

This file contains 179 comment letters received on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments. As noted in the Medicare Drug Price Negotiation Program: Revised Memorandum, Implementation of Sections 1191—1198 of the Social Security Act for Initial Price Applicability Year 2026 (the “revised guidance”), for comment letters from individuals not representing organizations, CMS has removed the name, address, and contact information of the individual for privacy purposes. Additionally, substantively duplicative comments (e.g., submitted as a part of a coordinated advocacy campaign) are combined into a single comment. Any organization, academic institution, or members of Congress or their staff have not been deidentified.

CMS received three substantively duplicative coordinated campaigns. The comment letter shown on page 2 had over 6,945 substantively duplicative comments. The comment letter shown on page 3 had over 155 substantively duplicative comments. The comment letter shown on page 4 had over 245 substantively duplicative comments.

CMS,

I was excited when the Inflation Reduction Act passed and Medicare was allowed to negotiate lower prices for key drugs. But I'm concerned about CMS' current plans for what Medicare drug price negotiation will actually look like:

I'm worried that using the current price of similar drugs as a starting point for negotiations will create too much of a bias in favor of the current — completely unfair — status quo that exists with Big Pharma monopoly pricing. Drug prices are already too high, so using current prices of alternative therapies as the starting point in negotiations will only ensure that drug prices stay too high.

Not only will using existing therapeutic alternative prices as a starting point bias negotiations towards prices that are too high, but taking this approach would also miss the opportunity for broader Medicare drug pricing impacts. If you successfully negotiate fair prices for Medicare, other manufacturers may start lowering prices for similar medications in order to stay competitive — further benefiting Medicare beneficiaries and taxpayers.

CMS should take a modified cost-plus approach, under which drug corporations are paid a fair portion of the revenue necessary to recover risk-adjusted R&D costs, accounting for therapeutic advancement, plus the marginal cost of production and distribution.

Please reconsider your approach to Medicare drug price negotiation and fight for lower drug prices, not the status quo that has led to our current prescription drug price crisis!

Thank you for your time.

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Dear Administrator Brooks-LaSure:

As an individual with a rare disease called Gaucher Disease. I have a very expensive infusion every 2 weeks.

I urge you to implement the Inflation Reduction Act (IRA) in a way that works for the rare disease community.

I have been getting this treatment for many years and will continue for as long as I live.

Key provisions in the IRA, including the \$2,000 annual and amortized monthly caps on out-of-pocket costs for Medicare Part D beneficiaries that start in 2025 will ensure that more rare disease patients will be able to afford the life-altering therapies they need.

At the same time, the vast majority of the more than 7,000 known rare diseases do not have an FDA approved treatment. This makes continued research and innovation especially important to the rare disease community. Unfortunately, the small patient populations and medical complexity associated with rare diseases creates unique challenges to rare disease drug development and can make determining a "fair price" difficult.

Here are three tangible ways CMS can better support the rare disease community in the implementation of the IRA:

1. Patients and caregivers have key insights on issues such as determining the value of a therapy and how it compares to potential alternate treatment options. I urge you to expand the opportunities available to patients to provide input into the negotiation process by making it easy for patients to submit data and organizing patient listening sessions specific to selected drugs to collect representative data while CMS is preparing the initial offer for a negotiated price.
2. Once a drug's price has been negotiated, it has been shown to be appropriately priced according to CMS; therefore it should be placed on a higher formulary tier to reduce patient out-of-pocket costs. In addition, CMS should require Medicare Part D plans to significantly reduce or eliminate utilization management tools, including step therapy and/or prior authorization barriers to ensure patients are able to quickly access a negotiated product because health care providers, in partnership with their patients, are best positioned to choose the right therapy.
3. Clarify that orphan drugs are exempt from price negotiations until the drug is actually FDA-approved and marketed for more than one disease. Otherwise CMS risks creating big disincentives for rare disease drug development.

Thank you for keeping the complex needs of the rare disease community in mind when implementing this law.

Sincerely,

A black rectangular redaction box covering the signature area.

Dear Administrator Brooks-LaSure,

As you implement the Inflation Reduction Act, please solicit feedback from patients, as they could be the ones negatively impacted from any unintended consequences of the law. Anything that results in fewer choices, higher costs, or reduced access to medicines will be unacceptable for patients.

I appreciate your attention to this issue.

Thank you,

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Submitted via email to IRARebateandNegotiation@cms.hhs.gov

April 14, 2023

Dr. Meena Seshamani, M.D., Ph.D.
Department of Health & Human Services
Centers for Medicare & Medicaid Services
Center for Medicare
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation Program Guidance

Dear Dr. Seshamani:

340B Health represents over 1,400 public and private nonprofit hospitals that participate in the 340B federal drug discount program. We appreciate the opportunity to provide comments on the Center for Medicare's guidance regarding implementation of Sections 1191-1198 of the Medicare Drug Price Negotiation Program for initial price applicability in 2026.¹

The guidance specially addresses how manufacturers will make the Maximum Fair Price (MFP) available to pharmacies, noting that the MFP does not need to be available to providers that participate in 340B ("covered entities"), for qualifying drugs dispensed to 340B eligible patients, except in situations where the MFP is lower than the 340B ceiling price.² Since the MFP does not need to be made available to covered entities, except in rare situations, we understand the CMS guidance will not interfere with current 340B operations, and that covered entities will continue to use their existing 340B purchasing and dispensing processes for their Medicare patients that qualify for 340B, and that manufacturers will continue to provide the 340B discount at the time that the covered entity purchases the drug. We strongly support this position.

For situations where the MFP is lower than the 340B ceiling price, the guidance states that the manufacturer is responsible for providing the covered entity the difference between the MFP and the 340B ceiling price.³ This could happen as a result of errors made by the manufacturer when calculating the 340B price, prompting a recalculation of the 340B ceiling price that would apply retroactively. It could also happen during the first two quarters that a new MFP price applies, as that price will not have factored into the 340B statutory formula as the "best price" for purposes of calculating the ceiling price until the third quarter. Processes used by 340B covered entities

¹ CMS, Medicare Drug Price Negotiation Program, Initial Memorandum, March 15, 2023, <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

² *Id.* at 32-33.

³ *Id.* at 33.

distinguish claims that qualify for 340B from those that do not and 340B covered entities maintain extensive accumulation and purchase records that distinguish between drugs purchased at 340B and at non-340B prices. As such, covered entities will have records to support the manufacturer's obligation to repay the difference between the 340B price and the MFP. This holds true for covered entity pharmacies as well as for their contract pharmacies, as records must be maintained to identify which dispenses were for 340B drugs and which were for non-340B drugs in those situations as well. Maintenance of these records are a core requirement of 340B, and are regularly enforced by the Health Resources and Services Administration (HRSA) in audits.

Thank you for considering our comments. Please feel free to reach out to me if you have any questions or if we can provide any additional information.

Sincerely,

A handwritten signature in black ink, appearing to read "Maureen Testoni".

Maureen Testoni
President & CEO

cc: Carole Johnson, Administrator, Health Resources and Services Administration

Rear Admiral Krista Pedley, Director, Office of Special Health Initiatives, Health Resources and Services Administration

Dr. Emeka Egwim, Director, Office of Pharmacy Affairs, Health Resources and Services Administration

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April 14, 2023

Meena Seshamani, M.D., Ph.D.
Director, Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services

Submitted electronically to IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Dr. Seshamani:

On behalf of our nearly 38 million members and all older Americans nationwide, AARP appreciates the opportunity to comment on the March 15, 2023, memorandum of proposed initial guidance pertaining to the implementation of the Medicare Drug Price Negotiation Program. AARP strongly supported the Medicare Drug Price Negotiation Program (hereinafter “Program”) and the other prescription drug-related policies contained in the Inflation Reduction Act of 2022 that will help address high prescription drug prices and costs. It is not fair or right to ask patients and taxpayers to continue paying for prescription drugs that have been priced based on what the market will bear. Successful implementation of the new federal law will help reduce prescription drug prices and costs and ensure that millions of older Americans are better able to access the prescription drugs they need at a price they can afford. It will also generate billions in savings for the Medicare program.

AARP commends CMS for soliciting input from the public on this guidance and appreciates its efforts to ensure that patients, caregivers, and health care providers have a voice in the negotiation process. AARP strongly believes that the needs of Medicare beneficiaries should remain paramount as the agency implements the Negotiation Program. To realize the savings that were intended, we encourage CMS to ensure that the negotiation process achieves the lowest possible maximum fair price (MFP) for each selected drug. It is also important for the agency to provide as much transparency as possible to help ensure that the public has confidence that MFPs are in fact fair and appropriate. CMS should place a high priority on conducting robust outreach and education for Medicare beneficiaries and health care providers to ensure that they are aware of the MFPs for selected drugs. These efforts should include clear, consumer-friendly reporting and appeals processes for when an MFP is not provided as required under the law.

AARP also strongly supports the collection and consideration of appropriate clinical evidence, including non-discriminatory drug value assessments, to inform CMS’ evaluations of selected drugs. We also support efforts to help ensure program integrity and reduce opportunities for drug companies to game the system.

While the statute that created the Program is broadly prescriptive, the agency is tasked with developing many specific details for the operation of the Program in a number of important areas. Below we offer more specific comments in response to the initial guidance.

Identification of Qualifying Single Source Drugs and Selected Drugs

AARP recognizes that section 30 of the initial guidance is considered final and not subject to comment, but nonetheless expresses its strong support for the agency's approach to establishing the date of approval or licensure that will determine when a drug is eligible for the negotiation process. By design, virtually all drug companies will have already made billions of dollars from selected drugs prior to the start of the negotiation process. Waiting 9 or 13 years, respectively, before an MFP for a traditional or biologic drug becomes available is already a very long period of time for beneficiaries and Medicare to be paying prices based on what the market will bear. Drug companies should not be given the opportunity to extend this period for longer.

AARP also supports CMS' approach to temporarily delay the selection of certain brand name biologic drugs for negotiation to protect against potential gaming of the selection process by drug companies. More specifically, AARP applauds CMS' approach that will assess whether there is a high likelihood that a competing biosimilar will enter the market in the two years after a brand name biologic drug becomes otherwise eligible for negotiation, which we believe will help curtail potential gaming of the system. AARP also appreciates that brand name biologic drug companies that enter into agreements with biosimilar drug companies that require or incentivize them to submit a delay request to CMS or restricts the quantity of the biosimilar that may be sold will not be able to benefit from this exemption. Such "pay for delay" gaming is well-known for its harmful impact on competition and helping to artificially maintain high prescription drug prices.

Supporting and Encouraging Further Transparency

AARP supports and strongly encourages transparency to the greatest extent possible in all aspects of the Program and especially throughout the negotiation process. While the statute limits how CMS can use or disclose propriety information, the statute nonetheless directs the agency to identify what information is in fact proprietary. AARP encourages the agency to consider, within the confines of the law, what is in the best interest of the Program and the public when determining which information is proprietary and to favor making relevant information publicly available whenever possible. This is especially important when the agency posts the MFP negotiated for a selected drug and its justification, where a high level of transparency will help instill confidence that the MFP represents the lowest price that the agency can reasonably obtain.

Negotiation Factors Regarding Therapeutic Alternatives and Consideration of Evidence from Any Interested Party

AARP supports CMS' decision to allow any interested party to submit data and evidence to CMS about therapeutic alternatives to drugs selected for negotiation. AARP agrees that

information from members of the public, including manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested parties, can play an important role in informing the agency's negotiating position. However, AARP is also extremely concerned that the amount of information that is submitted could be overwhelming and strongly encourages CMS to develop guardrails, potentially informed by best practices used by other health authorities, to help ensure that such input is meaningful and useful to the process.

AARP supports CMS' proposal to identify each FDA-approved indication for selected drugs and to identify therapeutic alternative(s) for each indication of the selected drug. We also agree that indications for therapeutic alternative(s) should include both FDA-approved indications *and* off-label uses that are supported by appropriate clinical evidence. In addition, AARP strongly supports CMS' decision to consider research on real-world evidence in Medicare-aged populations. AARP is aware that many prescription drugs are not tested under real-world conditions prior to FDA approval and appreciates the potential usefulness of this data in the negotiation process, and notes that CMS' interest could help encourage more drug companies to engage in such research.

AARP recognizes and supports the statutory prohibition against using evidence from comparative clinical effectiveness research that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. However, AARP believes that there are health measures that do not violate this prohibition and that non-discriminatory drug value assessments are an extremely valuable source of information, and strongly supports using as much of such research as possible in the negotiation process. AARP also supports CMS' intent to consider studies that clearly separate prohibited evidence from other evidence that is relevant to the negotiation process.

AARP broadly supports the definitions included in Appendix C of the guidance, as such terms are applied for purposes of the negotiation process.

Developing Maximum Fair Price

AARP supports the proposed starting points for the initial offer for the MFP, including using the Medicare Part D net price and/or Average Sales Price (ASP) of therapeutic alternative(s) (or, in the case of multiple therapeutic alternatives, the range of net prices or ASPs) as the starting point; and using the Federal Supply Schedule or Big Four Agency price as the starting point if there is no therapeutic alternative or if use of the net price or ASP would result in a starting point higher than the statutory ceiling price. In the case of drugs with multiple therapeutic alternatives, AARP encourages CMS to consider using the lowest net price or ASP of all the alternatives as the starting point for the initial offer to help ensure that the MFP is the lowest price possible. AARP strongly supports adjusting the starting point for the initial offer based on clinical benefit, which will help ensure that the MFP reflects the value of the selected drug to Medicare beneficiaries and subpopulations of interest. AARP appreciates the breadth of evidence that CMS intends to include in this process and urges CMS to consider including non-discriminatory drug value assessments when appropriate and available. AARP also strongly supports the considerations CMS outlined for comparing the effectiveness and clinical benefit between a selected drug and its therapeutic alternatives and believes the considerations to be meaningful comparison points. Specifically, AARP supports CMS' intent to consider health outcomes,

intermediate outcomes that indicate a change in health outcomes, validated surrogate endpoints that predict a relevant health outcome, patient-reported outcomes, and patient experience. We also support CMS' intent to prioritize studies focused on the impact of the selected drug and its therapeutic alternatives on individuals with disabilities, the elderly, individuals who are terminally ill, and other patient populations represented among Medicare beneficiaries. AARP encourages CMS to also prioritize studies with participants from diverse racial and ethnic backgrounds that, as of 2021, make up an estimated 26 percent of the Medicare population.

Additionally, AARP supports the method specified for adjusting the preliminary price based on manufacturer reported data, and believes the method described will encourage an informed and appropriate initial offer amount. Specifically, AARP supports CMS' decision to compare research and development (R&D) costs to the relevant drug company's global, total lifetime net revenue in order to determine whether it has recouped its R&D costs. AARP supports a downward adjustment to be applied to the preliminary price if the unit cost of production and distribution is lower than the preliminary price; if the discovery and development funding was received from Federal sources; if the average commercial net price is lower than the preliminary price; or, if the selected drug has patents and exclusivities that will last for a number of years.

AARP strongly encourages CMS to develop a stringent process for validating manufacturer-submitted data, as it is essential that data used to inform the negotiation process are as accurate and complete as possible.

Finally, AARP appreciates the information that CMS intends to publish on its website regarding MFPs, including an explanation for the final price, and strongly urges CMS to publish as much information as possible. A high level of transparency will help ensure that the public has confidence that MFPs are fair and appropriate.

Consumer Protection, Oversight, and Manufacturer Compliance

AARP supports strong program integrity protections for the Medicare Drug Price Negotiation Program and seeks to ensure that the negotiation process captures as many high-cost drugs as possible. Thus, we are concerned that selected drugs cannot be replaced if they subsequently face generic or biosimilar competition and are removed from the negotiation process. We believe that this requirement has created the potential for gaming of the system and encourage CMS to take such actions as it can, consistent with the statute, to capture as many selected drugs in the negotiation process as possible for each initial price applicability year.

AARP is also concerned with the agency's reliance on a Primary Manufacturer (the holder of the NDA/BLA) to ensure that Secondary Manufacturer(s) (listed as the manufacturer in the NDA/BLA that markets the drug under an agreement with NDA/BLA holder) make the MFP for a selected drug available to MFP eligible individuals. While we are encouraged that the guidance speaks to the issue, AARP urges CMS to regularly monitor whether manufacturers, be they primary or secondary, are fully compliant with their duties under the law and guidance with respect to all duties under the Program. If manufacturers are not fully compliant, then appropriate sanctions should be promptly implemented to foster compliance.

As noted earlier, AARP strongly encourages CMS to develop a simple, straightforward process for beneficiaries and health care providers to report instances when eligible individuals do not

receive the MFP, and to seek reimbursement for any overpayments. The agency should also develop clear, concise educational materials and conduct regular outreach to beneficiaries, health care providers patient advocacy groups, State Health Insurance Assistance Programs (SHIPs), Area Agencies on Aging, and Medicare Part D plan sponsors on the Program generally. CMS should seek feedback from consumer advocates and organizations that work with Medicare beneficiaries about best practices and should also consider more targeted efforts as needed.

Both the statute and the initial guidance require CMS to monitor bona fide marketing to determine whether a drug is a qualifying single source drug. That monitoring is designed to ensure that the presence in the market of a generic drug means that there is robust and meaningful competition in the market. AARP strongly urges CMS to monitor for unusually low market penetration for new generic drugs that does not represent meaningful competition for a high-cost drug that would have otherwise been subject to negotiation. Strong oversight of whether competition is in fact bona fide is one of the pillars of program integrity that will ensure the success of the Program in lowering costs of medicines for the Medicare program and its beneficiaries.

Finally, the civil money penalties (CMPs) that the statute imposes for violations of the Program agreements are essential enforcement mechanisms to help ensure the goals of the Program are realized. For example, it is important for the integrity of the negotiation process that the information submitted to CMS for purposes of those negotiations be both comprehensive and accurate. While the goal is for full and honest disclosure of the requisite information to CMS for the negotiation process, it is important that manufacturers know the financial implications of any failure to do so. AARP encourages the judicious use of CMPs to ensure integrity in the negotiation process.

We thank you for the opportunity to submit comments on the initial guidance for the Program and look forward to its strong implementation. For decades, people in this country have paid the highest prices in the world for prescription drugs – often three times higher than people in other countries. Now is the time to change that. Effective implementation of this Program will represent a major victory for families across the country who are struggling to afford their prescriptions. It will also help encourage and appropriately reward the development of truly innovative products. AARP stands ready to assist in any way with these and other efforts to bring down drug prices and help older Americans afford the medications and treatments they need.

If you have any questions, please do not hesitate to contact me or Gidget Benitez at gbenitez@aarp.org.

Sincerely,

A handwritten signature in black ink, appearing to read "David Certner", with a stylized flourish at the end.

David Certner
Legislative Counsel and Legislative Policy Director
Government Affairs

April 14, 2023

Submitted via Electronic Filing: *IRAREbateandNegotiation@cms.hhs.gov*

Dr. Meena Seshamani, M.D., Ph.D.

CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services, U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attn: PO Box 8016

Re: “Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments”

Dear Dr. Seshamani:

AbbVie Inc. (“AbbVie”) appreciates the opportunity to provide feedback on the March 15, 2023, memorandum issued by the Centers for Medicare & Medicaid Services (“CMS”), entitled *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments* (“Guidance”), which contains guidance on how CMS intends to implement the “Drug Price Negotiation Program” of the Inflation Reduction Act (“IRA”).

AbbVie is a biopharmaceutical company committed to discovering and delivering transformational medicines and products in key therapeutic areas, including immunology, oncology, neuroscience, eye care, virology, and women’s health. Through this patient-focused approach, AbbVie does more than just treat diseases—it aims to make a remarkable impact on people’s lives. Innovation for patients is the lifeblood of our company. Since AbbVie’s launch in 2013, we have invested approximately \$50 billion in research to discover, develop, and deliver new medicines to patients.

The United States currently leads the world in innovation and high-risk drug development, with credit to American biopharmaceutical manufacturers who make the necessary investments to develop new, safe, and effective medications. However, the Guidance impedes Congress’s incentives for the biopharmaceutical industry to develop and test new treatments that benefit all Americans and to engage in the critical development and collaborative efforts needed to benefit patients. In fact, the Guidance seeks to implement policies that even undercut the Biden Administration’s broader health care priorities, such as the President’s Moonshot initiative to reduce the deadly impact of cancer.¹ Accordingly, AbbVie is concerned that the IRA—particularly as implemented in the CMS Guidance—will stymie these efforts and have serious unintended consequences for innovation and for patient care.

We are also concerned that, in this Guidance, CMS contemplates agency action that is unconstitutional or not authorized by Congress. Specifically, CMS is not taking adequate time to develop the processes necessary to implement the IRA faithfully. For example, CMS intends not to comply with essential notice-and-comment rulemaking procedures even though it seeks to impose substantive obligations and restrict private rights in ways that extend far beyond the statute’s text and the authority granted by Congress. The Guidance contravenes clear statutory mandates, imposes new and unauthorized enforcement and data acquisition requirements,

¹ See Cancer Moonshot, *available at*: <https://www.whitehouse.gov/cancermoonshot/>.

violates manufacturers' First Amendment rights, interferes with private contractual arrangements, and fails to include provisions necessary to protect confidential trade secret information.

AbbVie's requests, objections, and recommendations are set forth below. We respectfully urge CMS to reconsider the Guidance, to respond meaningfully to feedback submitted, and to take the time needed to implement the IRA consistently with the statute's provisions and basic constitutional law requirements.

I. The Guidance Exceeds CMS's Statutory Authority for Determining Which Drugs Will be Subject to the "Drug Price Negotiation Program."

A. The IRA's Definition of a Qualifying Single Source Drug ("QSSD") Referring to a Bundle of Drug Products Renders the Entire "Drug Price Negotiation Program" Unworkable (Sections 30.1, 60.1, 60.2, 60.5).²

CMS interprets a QSSD to refer to:

- "For drug products, all dosage forms and strengths of the drug with the same *active moiety* and the same holder of a New Drug Application (NDA), inclusive of products that are marketed pursuant to different NDAs;" and
- "For biological products, all dosage forms and strengths of the biological product with the same *active ingredient* and the same holder of a Biologics License Application (BLA), inclusive of products that are marketed pursuant to different BLAs."³

In other words, each QSSD that CMS designates as a selected drug for price "negotiation" represents a bundle of all drug/biological products from the same NDA/BLA holder having the same active moiety/ingredient. CMS's interpretation that a QSSD refers to a bundle of drug products is *ultra vires*, violates the IRA's explicit requirements, and contravenes Congress's framework for selecting only a limited number of drug products each year.

CMS must comply with the definition of a QSSD provided in the IRA. Under the IRA, a "Drug Product" or "Biological Product" must satisfy several criteria to fall within the statutory definition of a QSSD: (i) it must be a product covered by Medicare Part B or Part D, (ii) it must be approved by the FDA for at least 7 years (for drugs) or licensed by the FDA for at least 11 years (for biologics), and (iii) it must not be the reference listed drug for an approved and marketed generic drug under FDCA § 505(j) or the reference product for an approved and marketed biosimilar under PHSA § 351(k).⁴ Drug and biological products that do not meet these statutory criteria cannot be QSSDs or selected drugs subject to the IRA's price controls.

The IRA's definition of a QSSD does not contemplate bundling different drug products as a single QSSD, nor does it mention using the "active moiety" or "active ingredient" to describe a QSSD. Indeed, the IRA's definition forecloses using an "active moiety" or "active ingredient" to delineate the scope of a QSSD. The relevant statutory language can be paraphrased as follows:

² AbbVie recognizes that CMS has not asked for feedback on section 30 of its Guidance, which CMS has deemed final. AbbVie is therefore not providing feedback on section 30 in its entirety and with respect to all of its provisions. Nonetheless, AbbVie reserves its rights, including its position that section 30's provisions are unlawful and not enforceable. Section 30 does not comply with the definition of QSSD provided in the statute and represents *ultra vires* action. CMS's failure to undertake public notice-and-comment rulemaking on this important provision is unlawful and violates constitutional requirements, and we have significant due process concerns. Since many pieces of the Guidance are based on CMS's erroneous interpretation of QSSD, we do address the effect this erroneous definition has on the entire "Drug Price Negotiation Program."

³ Guidance § 30.1 (emphasis added).

⁴ Social Security Act ("SSA") § 1192(e).

“[t]he term ‘qualifying single source drug’ means . . . a drug . . . that is not the listed drug for any [generic] drug that is approved and marketed under [FDCA § 505(j)].”⁵ Under FDCA § 505(j), the “listed drug” for a generic drug must be an FDA-approved finished drug product—not an active moiety.⁶ To be approved and marketed under FDCA § 505(j), a proposed generic drug must rely on a listed drug that, among other shared characteristics, has the same route of administration, dosage form, and strength as the proposed generic drug.⁷ Only finished drug products—not active moieties—exhibit such characteristics. Indeed, a proposed generic drug submitted for approval in an ANDA that relies solely on a particular active moiety as its listed drug—but which is agnostic as to dosage form, strength, and route of administration—could not be approved by FDA. Similarly, the PHSA defines a “reference product” for a biosimilar to mean “the *single biological product* licensed under subsection (a) against which a [biosimilar] biological product is evaluated in an application submitted under subsection (k).”⁸ Biosimilar products, like generic drugs, must also match the strength, route of administration, and dosage form of a “reference product” to be licensed and marketed under PHSA § 351(k).⁹ By cross-referencing the established definitions of a generic drug “approved and marketed under section 505(j)” of the FDCA and a biosimilar product “licensed and marketed under section 351(k)” of the PHSA, Congress purposefully defined a QSSD to refer to a specific referenced product—not its active moiety or active ingredient.

CMS’s misapplication of the IRA’s definition of a QSSD expands the scope of what constitutes a “selected drug,” rendering the process for negotiating a single “maximum fair price” (“MFP”) for such selected drug unworkable. The IRA instructs CMS to rank the negotiation-eligible QSSDs by the highest total expenditures to create the “selected drug” list.¹⁰ Then, the IRA directs CMS to “negotiate a maximum fair price for such [selected] drug.”¹¹ However, since CMS has interpreted a “selected drug” to represent a bundle of finished products containing the same active moiety or active ingredient, CMS must reconcile how this single MFP can be equitably applied across all dosage forms and strengths of such active moiety or active ingredient. As discussed in Section III below, CMS’s Guidance relies on complex and arbitrary formulas to aggregate prices across finished products, and then creates a single MFP to be applied across all dosage forms and strengths of the selected drug, and then further disaggregates the single MFP to determine what is the actual MFP provided to patients.¹² The IRA directs CMS to publish this MFP “for such [selected] drug negotiated with the manufacturer.”¹³ CMS apparently recognizes that establishing a single MFP across all dosage strengths and dosage forms of a selected drug in CMS’s QSSD bundle is unworkable. As such, CMS states that it “intends to publish the MFP at the per unit (e.g., tablet) level for each dosage form and strength associated with the selected drug.”¹⁴ CMS’s machinations to determine what is the single MFP for each selected drug, while still meaningfully informing patients of what MFP would apply to their drug product, directly results from CMS’s

⁵ SSA § 1192(e)(1).

⁶ 21 U.S.C. § 355(j)(2)(A)(i); see also 21 C.F.R. § 314.3(b) (defining a “listed drug” as “a new *drug product* that has been approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act for safety and effectiveness or under section 505(j) of the Federal Food, Drug, and Cosmetic Act, which has not been withdrawn or suspended under section 505(e)(1) through (5) or section 505(j)(6) of the Federal Food, Drug, and Cosmetic Act, and which has not been withdrawn from sale for what FDA has determined are reasons of safety or effectiveness”) (emphasis added).

⁷ FDCA § 505(j)(2)(A)(i), (iii).

⁸ 42 U.S.C. § 262(i)(4).

⁹ PHSA § 351(k)(2)(A)(i)(IV).

¹⁰ SSA § 1192(a), (c).

¹¹ SSA §§ 1193(a)(1), 1194(a)(1) (emphasis added).

¹² Guidance §§ 60.1, 60.2.2-4.

¹³ SSA § 1195(a)(1).

¹⁴ Guidance § 60.5.

disregard of Congress's commands, rewriting the definition of a QSSD to refer to a bundle of drug products having the same active moiety or active ingredient.

B. CMS's Guidance Undermines Innovation by Expanding the Scope of the IRA's Drug Price Controls Far Beyond What Congress Intended (Section 60.5).

The IRA limits the number of drugs that CMS may select for price setting each year—starting with 10 negotiation-eligible Part D drugs in the first year (2026) and increasing to 20 negotiation-eligible Part B and D drugs for the fourth year (2029) and beyond.¹⁵ CMS's approach, which impermissibly bundles together a manufacturer's finished products containing the same active moiety or active ingredient, contravenes Congress's framework for selecting only a limited number of drug products each year to subject to price controls. And once a single product in such a bundle has been approved for 7 years (or 11, in the case of a biological product), all products in the bundle would be potentially subject to price controls. CMS would "negotiate" a price that it would apply to each manufacturer's products having the same active moiety or active ingredient, including new products that have just been approved and launched, and even new products introduced after the Manufacturer Agreement is signed and the "negotiation" occurs.¹⁶ This defies Congress's manifest intent to restrict the IRA's price controls to only products that have been on the market for an extended period without generic or biosimilar competition. Sweeping newly approved drug products into the IRA's price controls would severely harm innovation in the biopharmaceutical industry—ultimately, to the detriment of patient care.

CMS's Guidance undermines the incentives Congress has provided for the biopharmaceutical industry to continue innovating around previously approved active moieties and active ingredients. Presently, continuing innovation is not only common in the biopharmaceutical industry but also a natural consequence of the modern drug approval paradigm. The research and development necessary to develop the first FDA-approved product with a novel active moiety or active ingredient is resource intensive and fraught with risk. As a result, an innovator company will often file its NDA/BLA with the FDA once it completes enough research and development to secure its first approval, even though it may have already started research and development on further improvements. This prioritizes getting safe and effective drug and biological products to patients as soon as FDA approval is possible. CMS's Guidance changes this paradigm. With CMS failing to honor the IRA's 7- and 11-year protections from drug selection, the timing of when and in which order a manufacturer seeks FDA approval first for a novel active moiety or active ingredient becomes significant.

Patients benefit from the continued investment by the biopharmaceutical industry to develop new and improved products of previously approved active moieties or active ingredients. For example, new dosage forms, strengths, and routes of administration may: (i) enhance effectiveness for the same or new indications—e.g., by providing for controlled release of the active ingredient, or new dosing regimens required for new indications; (ii) present a better adverse event profile—e.g., by reducing the incidence of injection site reactions for an injectable product; (iii) improve patient compliance—e.g., by reducing frequency of administration; and (iv) otherwise offer distinct advantages to specific patient groups. Healthcare professionals benefit from the flexibility to treat the individual needs of their diverse patients with a precise selection from a range of products, leading to better health outcomes.

FDA's annual review of new drug approvals highlights the significant benefits to patient health from the biopharmaceutical industry's innovation surrounding new formulations and dosage forms of previously approved active ingredients, including the following examples:

¹⁵ SSA § 1192(a).

¹⁶ Guidance § 60.5.1.

- “Tivicay PD (dolutegravir), tablets for oral suspension, approved in 2020 to treat HIV-1 infection in pediatric patients . . . Dolutegravir was originally approved by CDER in 2013 to treat HIV-1 infection in adults and children 12 years of age and older . . . This approval expands the patient population approved to use this drug to include much younger and smaller children—a *significant advance*; for babies and young children with HIV, getting treatment early is very important as HIV can progress more quickly in children than adults.”¹⁷
- “Baqsimi (glucagon), nasal powder, approved [in 2019] to treat patients with diabetes ages four and older who have severe hypoglycemia --- which occurs when a patient’s blood sugar level falls to a point where he or she becomes confused or unconscious or suffers from other symptoms that require assistance from another person to treat. [Glucagon was originally approved by FDA in 1960.] Until this approval, people suffering from a severe hypoglycemic episode had to be treated with a glucagon injection that first had to be mixed in a several-step process. *This new way to administer glucagon may simplify the process, which can be critical during an episode*, especially since the patient may have lost consciousness or may be having a seizure.”¹⁸
- “Cuvrior (trientine tetrahydrochloride) tablets were approved in 2022 with the previously approved active ingredient trientine to treat patients with stable Wilson’s disease, a genetic disorder in which excess copper builds up in the body. . . Cuvrior does not require refrigeration, unlike the original formulation of trientine [originally approved by FDA in 1985].”¹⁹

Subjecting newly approved products to price setting on account of the active moiety or active ingredient’s initial entry to the market undercuts the incentive to invest in developing these new products. Patients ultimately lose if the investment in continued innovation becomes too risky.²⁰

C. The Guidance Establishes an Unauthorized, *Ultra Vires* Process for CMS to Determine Which Drugs May Be Selected and When to Remove Drugs from the Selected Drug List (Sections 60.7, 70, 90.4).

The IRA is intended to focus on drugs that have been on the market for extended periods of time without any generic or biosimilar competition, and Congress intended for only those qualifying drugs that are truly “single source” to be subjected to the IRA’s “Drug Price Negotiation Program.” Under the IRA, a drug product that is the listed drug for any generic that is “approved and marketed” under FDCA § 505(j) or a biological product that is the reference product for any biosimilar that is “licensed and marketed” under PHSA § 351(k) is ineligible to be a QSSD.²¹ Similarly, a drug is removed from the selected drug list following CMS’s determination that an

¹⁷ FDA, Center for Drug Evaluation and Research, *Advancing Health Through Innovation: New Drug Therapy Approvals 2020* (Jan. 2021), at 37, available at <https://www.fda.gov/media/144982/download> (emphasis added).

¹⁸ FDA, Center for Drug Evaluation and Research, *Advancing Health Through Innovation: New Drug Therapy Approvals 2019* (Jan. 2020), at 37, available at <https://www.fda.gov/media/134493/download> (emphasis added).

¹⁹ FDA, Center for Drug Evaluation and Research, *Advancing Health Through Innovation: New Drug Therapy Approvals 2022* (Jan. 2023), at 25, available at <https://www.fda.gov/media/164429/download>.

²⁰ See Congressional Budget Office, Research and Development in the Pharmaceutical Industry, at 11, box 3 (April 2021), <https://tinyurl.com/bddtnbtX> (discussing how price controls would reduce incentives for innovation and decrease the number of new drugs that could be brought to market).

²¹ SSA § 1192(e)(1)(A), (B).

approved generic under FDCA § 505(j) or a licensed biosimilar under PHSA § 351(k) has been “marketed pursuant to such approval or licensure.”²²

CMS is moving far beyond Congress’s statutory framework and its authority as an agency by imposing a heightened requirement for a generic or biosimilar to be deemed “marketed.” Instead of performing the straightforward determination that Congress required, CMS has crafted a complex, extra-statutory scheme requiring “*bona fide* marketing” based on CMS’s evaluation of whether there has been “robust and meaningful” competition from a generic or biosimilar.²³ This is an impermissible overstep of CMS’s authority under the IRA.²⁴ CMS does not have the expertise to determine whether a generic or biosimilar creates enough “robust and meaningful” competition.

“Marketing” of a generic or biosimilar product is a well-established and well-defined term—it means the introduction or delivery for introduction into interstate commerce of a drug product. This concept of marketing is applied consistently in FDA and CMS regulations and guidance governing drug and biological products.²⁵ Indeed, in Appendix C of the Guidance, CMS adopts this definition of marketing for purposes of reviewing a selected manufacturer’s data under SSA §§ 1193(a)(4)(A) and 1194(e)(1) but not for purposes of determining when to remove drugs from the selected drug list under SSA § 1192(c)(1)(A).²⁶ Congress did not intend separate definitions of “marketing” for different parts of the statute. Nor did Congress grant CMS discretion to adopt a new definition of “marketing” that is inconsistent with its established meaning existing at the time of passage of the IRA.

Despite the statute’s plain meaning, however, CMS’s Guidance creates extra-statutory requirements under which CMS will give credence to a generic drug or biosimilar’s marketing only if it is “*bona fide*.”²⁷ CMS’s Guidance contends that “*bona fide*” marketing requires monitoring for “robust and meaningful competition,” which will include considering factors such as whether a generic drug or biosimilar is available for purchase “in sufficient quantities” and the drug’s market share.²⁸ Nothing in the statute contemplates such monitoring. Nor does the statute support the vague terms and arbitrary lines CMS seeks to draw by establishing metrics like “sufficient quantities” and “market share.”

²² SSA § 1192(c)(1)(A).

²³ Guidance §§ 60.7, 70, 90.4.

²⁴ Guidance § 90.4. See *Gonzales v. Oregon*, 546 U.S. 243, 257 (2006) (finding that the Attorney General lacked legal authority under the Controlled Substances Act to regulate medical practices); *Rapanos v. United States*, 547 U.S. 715 (2006) (finding EPA lacked the power to regulate wetlands under the Clean Water Act because they did not qualify as “navigable waters”).

²⁵ See, e.g., 21 C.F.R. § 314.3 (defining “commercial marketing” as “the introduction or delivery for introduction into interstate commerce of a drug product described in an ANDA, outside the control of the ANDA applicant”); 21 C.F.R. § 330.14(b)(2) (describing market history requirements for inclusion in the OTC drug monograph system); see also *Sandoz, Inc. v. F.D.A.*, 439 F. Supp. 2d 26 (D.D.C. 2006) (explaining that the date the generic manufacturer began distributing its generic drug constituted “the first commercial marketing of the drug” and triggered the start of the generic manufacturer’s 180-day exclusivity); Medicaid Drug Rebate Data Guide for Labelers § 4.15 (August 2018) (“Market Date: For S, I, and N drugs marketed under an FDA-approved application (e.g., BLA, NDA, ANDA), the earliest date the drug was first marketed under the application number by any labeler.”); National Drug Rebate Agreement Between HHS and the Manufacturer, 83 Fed. Reg. 12,784 (Mar. 23, 2018) (“‘Marketed’ means that a covered outpatient drug is available for sale by a manufacturer in the states.”).

²⁶ Guidance at Appendix C (“‘Marketing’ is defined as the introduction or delivery for introduction into interstate commerce of a drug product.”).

²⁷ Guidance §§ 60.7, 70.

²⁸ Guidance § 90.4.

CMS also intends to review Medicare Part D Prescription Drug Event (“PDE”) data as a proxy to determine whether there has been *bona fide* marketing of a generic or biosimilar. This proxy is inappropriate, because it is not indicative of broader market realities beyond the Medicare program and, therefore, not a reliable indicator of when a drug is marketed.²⁹ A generic or biosimilar product may be marketed but have little Part D utilization. This could result from a time lag associated with securing placement on Part D formularies or difficulties negotiating for Part D formulary inclusion. There are other data sources CMS itself has available that indicate whether a drug is being marketed, such as the National Average Drug Acquisition Cost (NADAC) for Medicaid Covered Outpatient Drugs survey, which CMS updates weekly for generic drugs.³⁰

Also, CMS arbitrarily focuses on looking back at 12 months of data to determine whether a generic or biosimilar manufacturer has engaged in *bona fide* marketing.³¹ CMS fails to explain why a 12-month period is appropriate for this determination. The IRA clearly requires that, in order for a drug to be considered multi-source, the generic or biosimilar product will have been marketed at the time of CMS’s determination—not that the generic or biosimilar has met some undefined level of market performance over an arbitrary length of time.

D. CMS Should Be Transparent About the Process by Which a Drug Product Is Deemed a Selected Drug and Eventually Exits the Selected Drug List.

CMS’s Guidance is devoid of much-needed certainty and transparency, depriving stakeholders of meaningful opportunity to engage throughout the process. For example, under CMS’s Guidance for initial price applicability year (“IPAY”) 2026, manufacturers of selected drugs will not have certainty of which drug products will be subject to the “Negotiation Program” until September 1, 2023, giving them a mere 30 days to collect required information and determine whether to sign the Manufacturer Agreement or be subject to an exorbitant excise tax.

AbbVie urges CMS to ensure additional transparency along all steps of this process, including by publishing (1) its supporting calculations regarding how it determined the list of selected drugs; (2) for both newly selected drug products and drug products that remain on the selected drug list, its determinations that those drug products are not the listed drug or reference product for an approved and marketed generic or a licensed and marketed biosimilar; and (3) how those determinations were reached. In addition, CMS should ensure transparency with respect to delay requests of biosimilar manufacturers by publishing a list of biosimilar manufacturers submitting an Initial Delay Request, including the date by which CMS will approve or reject those requests, and by making CMS’s delay decisions known publicly. Taking those steps is critical to ensure predictability and accountability in the process. Moreover, because reference product sponsors are potentially liable for rebates under the biosimilar delay provisions, they should have notice and an opportunity to comment before a delay is granted or denied.

II. The “Negotiation” Process Is Not Properly Designed to Result in a Fair Negotiation.

AbbVie is concerned that both the IRA and CMS’s Guidance characterize the IRA’s price-setting provisions as creating a “negotiation” process when, in reality, they provide no meaningful opportunity for manufacturers to develop and submit information to influence CMS’s decisions.

²⁹ Guidance §§ 30.1, 70.

³⁰ <https://www.medicaid.gov/medicaid/prescription-drugs/retail-price-survey/index.html>.

³¹ Guidance §§ 30.1, 70.

A. The Guidance’s Process to Establish a Single Maximum Fair Price Exceeds CMS’s Authority and Contravenes Congress’s Intent (Sections 60.1, 60.4, 60.5).

The IRA directs CMS to generate a single MFP per drug,³² which is inconsistent with CMS’s interpretation of QSSD. Due to this erroneous interpretation, CMS has proposed distorting pricing metrics by aggregating across products, generating an overarching MFP, and dividing up this metric using complex and arbitrary formulas.³³ That approach exceeds CMS’s authority, violates the statute’s express mandates, and contravenes Congress’s intent.

It is also concerning that CMS intends to base the single price on the cost of the selected drug per 30-day equivalent supply, weighted across dosage forms and strengths, instead of per unit (e.g., a tablet, capsule, injection, or per volume or weight-based metric) for the purposes of determining a single price included in an initial offer.³⁴ This approach does not reflect patients’ true experiences, including how many doses a patient must take, side effects, efficacy, adherence, and other factors that significantly influence patient outcomes. For many drugs, a 30-day supply differs from patient to patient depending on any number of factors, such as patient weight, severity of condition, and the indication for which the product is prescribed. Many drugs also require ramp-up protocols or frequent changes in dosage, and other medicines are only utilized by patients on an as-needed basis. Moreover, CMS would be treating an active moiety (or active ingredient) as though it is the same across different types of delivery, which also does not reflect the patient experience—nor does it reflect the differing costs across delivery devices, which sometimes can be significant (e.g., the cost difference between an on-body injector and a prefilled syringe, or a complex ophthalmic dispenser versus a vial).

In addition, CMS’s proposal to determine a single 30-day equivalent supply by volume weighting multiple price points based on the presentations’ Medicare Part D utilization during the 12-month period ending May 31, 2023, does not reflect real world experience. Because this weighting does not correct for any of the patient-specific conditions noted above, it could result in a price point that is not reflective of actual cost or value of any specific presentation, but rather a split-the-difference average that undervalues some presentations while overvaluing others.

B. The Methodology for Developing an Initial Offer is Also Flawed (Sections 60.2, 60.3).

Similarly concerning, CMS is relying on flawed reasoning when developing an initial offer by “(1) identify[ing] therapeutic alternative(s), if any, for the selected drug . . . (2) us[ing] the Part D net price . . . and/or the Part B average sales price (ASP) for the therapeutic alternative(s) . . . (3) evaluat[ing] the clinical benefit of the selected drug (including compared to its therapeutic alternative(s)) . . . and (4) further adjust[ing] the preliminary price by the negotiation factors outlined in section 1194(e)(1) of the Act.”³⁵

The statute requires that the ceiling “*for the MFP* for a selected drug shall not exceed the lower of . . . an amount equal to the sum of the plan specific enrollment weighted amounts; or . . . an amount equal to the applicable percent, with respect to the selected drug, of the average [inflation-adjusted 2021] non-FAMP.”³⁶ In the Guidance, however, CMS states that it intends to have the *starting point for the initial offer* capped at the *MFP* ceiling price. CMS would take this approach, even if the price for a therapeutic alternative is higher—or, if there is no therapeutic alternative, if the Federal Supply Schedule/“Big Four” price is higher. Nothing in the statute authorizes CMS to impose a new requirement that the steps *within the initial offer* process cannot

³² See, e.g., SSA §§ 1191(c)(3) and 1194(c); Guidance §§ 60.1, 60.5.

³³ *Id.*

³⁴ *Id.*

³⁵ Guidance § 60.3.

³⁶ Guidance § 60.2.1 (emphasis added).

include prices higher than the *MFP* ceiling price—only that the ultimate MFP cannot be higher than the MFP ceiling price (and CMS has not undertaken the notice-and-comment rulemaking procedures that would be required to impose such a requirement). This approach not only runs afoul of statutory intent, but it also could result in unintended consequences that do not reflect the reality of market dynamics.

CMS states that it will *penalize* manufacturers by *decreasing* the initial price offer for selected drugs whose research and innovation has been recognized with the award of patents and FDA exclusivities.³⁷ As an example, CMS states that “if the selected drug has patents and exclusivities that will last for a number of years, CMS may consider adjusting the preliminary price downward.”³⁸ This policy repudiates the foundation under which the United States’ robust biopharmaceutical industry was built. CMS’s Guidance presents a clear and direct conflict with the purpose of the patent system to promote innovation and the purpose of the federal regulatory schemes conferring FDA exclusivities to encourage drug development. CMS’s Guidance harms those manufacturers that have invested in innovative research and development. This serves to blunt the incentive for manufacturers to continue to innovate and publicly disclose their inventions in patent applications. Similarly, CMS’s Guidance would serve to actively disincentivize the areas for which Congress has tried for years to incentivize biopharmaceutical research and development, including pediatric research, orphan drugs, and antibiotics. Pediatric exclusivity, and the children that Congress sought to help by incentivizing research and development for new products intended to treat pediatric patients, are in particular harmed by CMS’s approach, because the pediatric exclusivity runs after the expiry of any patent and regulatory exclusivity listed in the FDA’s Orange Book—the same period of time that the selected drug would be impacted by the IRA’s price controls. Perversely, CMS’s Guidance will penalize manufacturers for conducting those clinical studies in young children for which pediatric exclusivity is granted. CMS’s policy would thus punish—not reward—the investments in research and development that improve care for patients, in particular pediatric patients.

In addition, as CMS examines available evidence about therapeutic alternatives as the basis for determining offers and counteroffers, we note that therapeutic alternatives will almost invariably be indication specific. CMS should take into consideration whether a therapeutic alternative is medically appropriate for the same group of patients, and not just rely on the Part D net price and/or ASP of therapeutic alternatives for a selected drug (which itself has been inappropriately bundled across all formulations). All decisions should be driven by clinical guidelines, real world practice, and evidence-based medicine. The Guidance states that CMS intends to consider whether the product “represents a therapeutic advance compared to existing therapeutic alternatives”³⁹ and whether it fills an “unmet medical need.”⁴⁰ CMS should be aware that these determinations are extremely complex scientifically and have significant implications for the FDA approval process, comparative efficacy claims, labeling and promotion, and more.

C. The Process Is Not a True “Negotiation” and Does Not Adequately Engage Manufacturers or Account for Patient Experiences (Sections 50, 60.3, 60.4).

Unfortunately, the “negotiation factors” and “negotiation process” outlined in the Guidance amplify the unconstitutional nature of the IRA’s “Drug Price Negotiation Program.” The factors and the vague “process” provided do not allow for meaningful engagement from manufacturers and other critical stakeholders, and they do not adequately account for true patient experiences. To have a meaningful process, CMS should engage with manufacturers—along with other

³⁷ Guidance § 60.3.4.

³⁸ *Id.*

³⁹ Guidance § 50.2.

⁴⁰ *Id.*

stakeholders, such as health care providers—to define important outcomes and appropriate therapeutic alternatives. From a clinical perspective, manufacturers should also be able to provide information and evidence as it relates to the totality of a selected drug product. Furthermore, CMS should provide more transparency into the criteria CMS will utilize to identify academic experts, clinicians, and other interested parties who may weigh in on therapeutic alternatives, and it should have a transparent and even-handed process if the public disagrees with CMS’s selection of these experts.

Also troubling, CMS has said that it intends to offer only up to three meetings with manufacturers, and only if the manufacturer’s written counteroffer is not accepted by CMS. In other words, CMS intends to conduct the “negotiation process” using arbitrary benchmarks and without accepting adequate feedback from manufacturers or other stakeholders. This lack of ability for manufacturers to engage with CMS in a meaningful way is especially alarming because manufacturers of selected drugs must “agree” to “negotiate” or otherwise be subject to an excessive excise tax. This not only emphasizes the concerns around lack of proper process, but it also highlights that the process is not a true negotiation.

III. The Guidance Mandates Unreasonable Obligations on Primary Manufacturers.

CMS intends to enter into “Medicare Drug Price Negotiation Program Agreements” not with *all* manufacturers of selected drugs, but only with those manufacturers that hold the NDA(s) or BLA(s) for selected drugs, deemed the “Primary Manufacturers.”⁴¹ The Guidance also dictates that the Primary Manufacturer will be held liable for any failure by a Secondary Manufacturer to provide its information to the government and to make the MFP available to eligible individuals.⁴²

CMS has departed from the statutory definition of “manufacturer” by determining that a single “Primary Manufacturer” will be responsible for fulfilling the statutory “requirements” for any selected drug, including by providing information held by third parties. Nothing in the IRA distinguishes between “Primary Manufacturers” and “Secondary Manufacturers.” To the contrary, the statute states: “[t]he term ‘manufacturer’ has the meaning given that term in section 1847A(c)(6)(A) [of the SSA].”⁴³ That definition cross-references section 1927(k)(5) of the SSA, which defines a manufacturer as:

any entity which is engaged in—

(A) the production, preparation, propagation, compounding, conversion, or processing of prescription drug products, either directly or indirectly by extraction from substances of natural origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis, or

(B) in the packaging, repackaging, labeling, relabeling, or distribution of prescription drug products.

⁴¹ The guidance defines a “Primary Manufacturer” as the entity that holds an NDA(s)/BLA(s) for the selected drug, and it defines a “Secondary Manufacturer” as any other entity that meets the statutory definition of manufacturer for a drug product included in the selected drug and that either (1) is listed as a manufacturer in an NDA or BLA for the selected drug or (2) markets the selected drug pursuant to an agreement with the Primary Manufacturer. The definition for a Secondary Manufacturer also includes any manufacturer of any authorized generics and any re-packer or re-labeler of the selected drug that meet these criteria. Guidance § 40.

⁴² See Guidance § 90.2.

⁴³ SSA § 1191(c)(1).

Such term does not include a wholesale distributor of drugs or a retail pharmacy licensed under State law.⁴⁴

The Guidance departs from this statutory definition clearly referenced in the IRA.

It is concerning that CMS's Guidance seeks to impose binding requirements that Congress did not intend. The Guidance makes the Primary Manufacturer responsible to CMS when it signs an "agreement" to "negotiate" with the Secretary (or else be subject to a steep excise tax), and for not only its own information and conduct, but also that of every Secondary Manufacturer. CMS's Guidance does not provide any mechanism for Primary Manufacturers to collect information from Secondary Manufacturers or to control the prices at which Secondary Manufacturers sell their goods. While we understand that an entity required to comply with certain laws must make sure its agents or subcontractors comply with those laws as well, relationships between Primary and Secondary Manufacturers are not the same as those of entities and their agents. Even for those Primary and Secondary Manufacturers that do have an existing contractual relationship, CMS's Guidance risks irreparable harm by transforming those parties' relationships and rendering their existing contracts effectively void.⁴⁵ There is no evidence that Congress intended to authorize CMS to transform the pharmaceutical industry's ability to engage in private contractual relations.

We are also concerned that CMS cannot guarantee the confidentiality of Secondary Manufacturers' proprietary information because, under the Guidance, the Primary Manufacturer will be the conduit for the submission of the Secondary Manufacturer's information. Requiring the Secondary Manufacturer to provide its data to the Primary Manufacturer strips the Secondary Manufacturer of its proprietary information, and CMS cannot guarantee the confidentiality of the Secondary Manufacturer's proprietary data. The government cannot ensure that proprietary information "shall be used only by the Secretary"⁴⁶ and simultaneously require that it be turned over to (and verified for completeness by) a manufacturer's direct competitor.

The forced transfer of such highly sensitive data between private firms also raises anti-competitive concerns, especially when the Primary Manufacturer and Secondary Manufacturer are direct competitors. Indeed, re-packaged/re-labeled drugs often compete with branded products, and manufacturers of authorized generics often launch their own non-authorized generic drugs and end up in fierce competition with NDA-holding manufacturers. Critical pricing data are rarely shared between brand and authorized generic manufacturers for competitive and antitrust reasons, and the unauthorized disclosure of such information would result in far-reaching, irreparable harm. CMS recognized these concerns in the 2016 line extension rule when it backed away from a similar conflation of Primary and Secondary Manufacturers.⁴⁷ There is no reason it should take a different approach under the IRA, a statute that does not authorize CMS to distinguish between Primary and Secondary Manufacturers, let alone authorize CMS to impose

⁴⁴ Codified at 42 U.S.C. § 1396r-8(k)(5).

⁴⁵ See *E. Enterprises v. Apfel*, 524 U.S. 498, 523, 527 (1998) (plurality) (economic regulation that interferes with a contract or "investment-backed expectations" may affect a taking); *id.* at 547 (Kennedy, J., concurring) (economic regulation with retroactive effect may violate due process).

⁴⁶ SSA § 1193(c).

⁴⁷ "We are persuaded by the comments regarding the concerns associated with sharing of pricing data between competing manufacturers and have changed our position concerning the inclusion of another manufacturer's pricing data in the calculations of the additional rebate for line extension drugs. We also recognize the challenges of obtaining pricing information from non-related manufacturers, based on the comments received. Therefore, we are applying the line extension obligations to drugs that are manufactured by the initial brand name listed drug company and any other companies that have a corporate relationship with the manufacturer of the initial brand name listed drug." 81 Fed. Reg. 5170, 5267 (February 1, 2016).

obligations on NDA-holding manufacturers to be responsible for obtaining sensitive, proprietary information from competitors.

IV. The Guidance Raises Concerns Regarding Treatment of Proprietary Information.

CMS's Guidance improperly threatens to strip manufacturers of their rights in their own confidential trade secret and proprietary information. Numerous provisions call for the submission of confidential and trade secret information beyond what the IRA authorizes. While CMS's Guidance states that it intends, for IPAY 2026, to treat certain data elements submitted by a Primary Manufacturer as confidential,⁴⁸ AbbVie has concerns with what data will be protected and how that data may be used and disclosed. The absence of adequate guidelines raises significant concerns, because disclosure could result in significant and irreparable harm.

A. CMS Must Ensure, with Deference to Manufactures, That Proprietary Information Is Used Only for Purposes of Carrying Out the "Drug Price Negotiation Program" (Section 40.2.1).

The IRA provides that proprietary information (as determined by the Secretary) that a manufacturer submits "shall be used only by the Secretary or disclosed to and used by the Comptroller General of the United States for purposes of carrying out the [Negotiation Program]."⁴⁹ CMS acknowledges that "proprietary information, including trade secret and confidential commercial or financial information, is protected from disclosure under Exemption 4 of the Freedom of Information Act (FOIA) (5 U.S.C. § 552(b)(4))."⁵⁰ CMS also notes that it "intends to implement a confidentiality policy that is consistent with existing requirements for protecting proprietary information, such as Exemption 4 of FOIA. CMS intends to strike an appropriate balance between (1) protecting the highly sensitive information of manufacturers and ensuring that manufacturers submit the information CMS needs for the Negotiation Program and (2) avoiding treating information that does not qualify for such protection as proprietary."⁵¹

AbbVie agrees with CMS's plans to implement a confidentiality policy that is consistent with existing legal and regulatory requirements, including Exemption 4 of FOIA. AbbVie also agrees that non-public, confidential business information should be treated as proprietary. That would include, at a minimum, the non-FAMP of the selected drug, and the specific data elements described in Appendix C of the Guidance regarding research and development costs and recoupment, unit costs of production and distribution, pending patent applications, market data, and revenue and sales volume data. There also could be other confidential, proprietary, and trade secret information that manufacturers might provide to CMS as part of the "Drug Price Negotiation Program." For example, the IRA also requires the manufacturer of a selected drug to submit to the Secretary "information that the Secretary requires to carry out the negotiation (or renegotiation process)" under the "Negotiation Program."⁵² These technical and commercial data are proprietary information whose public disclosure could present a substantial risk of serious harm to manufacturers' operation for the selected drug and its other related assets.

Therefore, AbbVie strongly urges CMS to afford manufacturers deference in making case-by-case, good-faith determinations as to the proprietary information that must be protected from public disclosure and subject to the protections around its use, as set forth in the IRA. In most cases, only the manufacturer—as the submitter of the information—will be able to make reasonable determinations as to whether any specific data provided to the Agency are trade

⁴⁸ See Guidance § 40.2.1.

⁴⁹ SSA § 1193(c).

⁵⁰ Guidance § 40.2.1.

⁵¹ *Id.*

⁵² SSA § 1193(a)(4); *see also* Guidance § 40.2.

secrets or confidential commercial or financial information. Manufacturers must have confidence that their good faith determinations regarding proprietary information will be upheld by CMS, especially with respect to any information that is not already publicly available. Otherwise, if CMS were to disclose such confidential, proprietary information to the public, manufacturers would suffer irreparable harm without any ability to seek an adequate remedy. This harm could extend beyond the specific selected drug and affect confidential technical and commercial information concerning other assets of the manufacturer. This harm is preventable. Accordingly, CMS should treat as proprietary any non-public information that a manufacturer provides to CMS as a part of the “negotiation process” that the manufacturer reasonably believes to constitute, and designates as, its proprietary information.

CMS should take meaningful steps to ensure that any proprietary information is used only for purposes of carrying out the “Negotiation Program,” consistent with the terms of the IRA.⁵³ CMS should also ensure that its information technology security systems and processes are sufficient to protect the information from unauthorized use, disclosure, viewing, or dissemination.

B. CMS Should Adopt Safeguards to Protect Against the Disclosure of Confidential Information When Publishing an Explanation of the MFP (Section 40.2.1).

Under section 1195(a)(2) of the SSA, as added by the IRA, the Secretary is required to publish an explanation for the MFP. CMS’s Guidance states that, in publishing this explanation, it “intends to make high-level comments about the data submitted to CMS, without sharing any proprietary information reported to CMS. . . for purposes of the negotiation.”⁵⁴ As an example, CMS offers that it “does not intend to make public the research and development costs reported by a Primary Manufacturer, as CMS would treat that data as proprietary, but CMS may say ‘the manufacturer has recouped its research and development costs.’”⁵⁵

AbbVie acknowledges CMS’s mandate under the IRA to publish an explanation for the MFP. However, AbbVie is concerned with the high potential for inadvertent disclosure of proprietary information through these published explanations. These explanations could also create or perpetuate inaccurate impressions or conclusions about a manufacturer and its proprietary information. That is particularly true when the comments are meant to be “high-level” and therefore by-design cannot include enough context or detail to provide a proper explanation for such a complex process.

Accordingly, AbbVie respectfully requests that before publishing an explanation (or otherwise disclosing information that a manufacturer has designated confidential and proprietary), CMS provide manufacturers a “pre-release review” so they may review and object to the Agency’s proposed explanations. Not only would such a notification help avoid any inadvertent or inaccurate disclosure of proprietary information, but it also would be consistent, for example, with regulations that govern FOIA requests involving confidential commercial information.⁵⁶ It also would be consistent with the practices of FDA in handling trade secret and confidential commercial information.⁵⁷ As noted, any information included in CMS’s public explanations of MFP could be proprietary, and we believe it is important that manufacturers be afforded an opportunity to review the explanations and object to the inclusion of any proprietary information.

⁵³ See Guidance § 40.2.1.

⁵⁴ *Id.*

⁵⁵ *Id.*

⁵⁶ See 45 C.F.R. § 5.42 (requiring data submitters be provided 10 working days from the date of the FOIA request notice to object to disclosure of any part of the records and to state all bases for their objections).

⁵⁷ See 21 C.F.R. §§ 20.61, 314.430.

C. CMS's Guidance Violates the Constitution by Prohibiting Manufacturers from Disclosing Information and Requiring Document Destruction (Section 40.2.2).

The IRA directs the Secretary to enter into “Manufacturer Agreements” under which “the manufacturer complies with requirements determined by the Secretary to be necessary for purposes of administering the program and monitoring compliance with the program.”⁵⁸ CMS relies on this vague grant of authority to impose mandatory non-disclosure and information destruction requirements on manufacturers that violate the First Amendment.⁵⁹

Specifically, the Primary Manufacturer is barred from disclosing “any information in the initial offer or any subsequent offer by CMS, the ceiling price contained in any offer, or any information contained in any concise justification provided with an offer,” as well as “any information exchanged verbally during the negotiation period.”⁶⁰ In addition to preventing manufacturers from speaking truthfully about the “negotiation” process, CMS also requires that manufacturers destroy information if the drug or biologic no longer qualifies as a selected drug.

Nowhere in the IRA does Congress authorize CMS to impose this forced gag order on manufacturers. CMS's mandatory non-disclosure and information-destruction provisions impede manufacturers' rights to free speech and are not necessary to administer or monitor compliance with the “Negotiation Program.” CMS provides no explanation as to why this proposal would be permitted under the IRA as “necessary for purposes of administering the program.”⁶¹

CMS's Guidance exacerbates First Amendment concerns by silencing any dissenting or even neutral information sharing about the “negotiation” process. Courts find compelled speech even more objectionable than censorship because those who are forced to speak are “coerced into betraying their convictions.”⁶² The Guidance *both* compels speech *and* censors speech. Indeed, because prior governmental restraints on speech “are the most serious and the least tolerable infringement on First Amendment rights,”⁶³ they are subject to a “heavy presumption against [their] constitutional validity.”⁶⁴ That principle applies with special force to restraints on the disclosure of “truthful information about a matter of public significance”—such as the data subject to use restrictions in section 40.2.2. Those types of restrictions are almost never permissible under the First Amendment.⁶⁵

AbbVie is unaware of any price negotiation with the government in which a private party is compelled to destroy its records once the negotiation is complete. Moreover, this absurd practice would harm manufacturers and put them at an unnecessary disadvantage. Contrary to CMS's suggestion that document destruction would be necessary for purposes of administering the program, CMS's proposed Guidance would serve to hinder the program's administration and efficiency. Retaining information about the process will help make any “negotiation” of subsequent selected drugs more efficient—especially as CMS and manufacturer personnel change over time. Retaining this information would also help to ensure that CMS remains consistent in its determination of MFP across a manufacturer's drugs or biologics. Therefore, record destruction serves no understandable purpose in an alleged “fair negotiation process.”

⁵⁸ SSA § 1193(a)(5).

⁵⁹ See Guidance § 40.2.2.

⁶⁰ *Id.*

⁶¹ SSA § 1193(a)(5).

⁶² *Janus v. Am. Fed'n of State, Cnty., & Mun. Emps.*, Council 31, 138 S. Ct. 2448, 2464 (2018).

⁶³ *Nebraska Press Ass'n v. Stuart*, 427 U.S. 539, 559 (1976).

⁶⁴ *Org. for a Better Austin v. Keefe*, 402 U.S. 415, 419 (1971) (quotation marks omitted).

⁶⁵ *Bartnicki v. Vopper*, 532 U.S. 514, 527 (2001).

V. The Guidance Lacks Adequate Operational Safeguards for Effectuating the MFP.

The Guidance does not provide enough information about how CMS intends to implement two critical operational complexities presented by the IRA: (1) how manufacturers are to “provide access” to the MFP to MFP-eligible individuals; and (2) how this access can be achieved without violating the 340B nonduplication provision of the statute.⁶⁶

A. CMS’s Guidance Does Not Contain Safeguards Necessary to Ensure That the MFP Is Provided to Only Eligible Individuals (Section 40.4).

The Guidance does not contemplate adequate safeguards to ensure that the MFP is made available only to eligible individuals. For example, CMS does not consider that manufacturers and/or third-party administrators (“TPAs”) need access to sufficient claims-level data for in order to validate MFP-eligibility. Absent legitimate procedures to ensure that access to the MFP be limited only to those individuals entitled to that price—consistent with the clear statutory language⁶⁷—the program risks operational failure and substantial abuse. CMS should be clear to participating dispensaries that diversion will not be tolerated, and it should establish a manufacturer right to audit dispensaries for appropriate use and distribution of units purchased at the MFP.

Further, the requirement for timely reimbursement within 14 days, as proposed in the Guidance (but not in the statute), is insufficient to obtain data, validate claims, and process appropriate reimbursements. In other government programs requiring eligibility verification and rebating, the timetable for rebates is more than twice as long (38 days in the Medicaid Drug Rebate Program and 38 days in the Part D Coverage Gap Discount Program).⁶⁸

Additionally, CMS’s Guidance fails to recognize that manufacturers typically do not have existing contractual relationships with the roughly 60,000 retail dispensers (e.g., pharmacies) across the U.S.⁶⁹ In most cases, this Guidance would require manufacturers to develop entirely new contracts, financial relationships, data systems, and other capabilities, to provide the MFP only to eligible individuals. Given the existing complexity in the biopharmaceutical supply chain, CMS’s Guidance would have done well to consider existing contractual relationships and processes that could have been leveraged to reduce the complexity, confusion, and burden of providing the MFP.

B. CMS’s Guidance Does Not Contain Safeguards Necessary to Avoid 340B Duplication.

The statute is clear that manufacturers shall not be required to provide access to the MFP and the 340B discount on the same unit.⁷⁰ Rather, manufacturers of selected drugs must provide

⁶⁶ Guidance § 40.4.

⁶⁷ Individuals entitled to the MFP must be “enrolled in a prescription drug plan under part D . . . or an MA-PD plan under part C.” SSA § 1191(c)(2).

⁶⁸ See 42 CFR § 423.2315(b)(3) (providing requirements for the Medicare Coverage Gap Discount Program Agreement); CMS, Medicaid Drug Rebate Program Notice, Release No. 89 (March 10, 2014), available at: <https://www.medicaid.gov/medicaid-chip-program-information/by-topics/prescription-drugs/downloads/rx-releases/mfr-releases/mfr-rel-089.pdf> (noting that “manufacturers have 37 calendar days (as evidenced by the postmark by the U.S. Postal Service on the envelope) to pay rebates before interest begins to accrue”).

⁶⁹ See Commonwealth Fund, *Competition, Consolidation, and Evolution in the Pharmacy Market*, available at: <https://www.commonwealthfund.org/publications/issue-briefs/2021/aug/competition-consolidation-evolution-pharmacy-market#:~:text=Of%20the%20roughly%2060%2C000%20retail,percent%20of%20retail%20prescription%20revenues> (Aug. 12, 2021).

⁷⁰ See SSA § 1193(d).

the lower of the MFP or the 340B price to individuals who are eligible for both. Many factors complicate application of this nonduplication requirement:

- 340B-covered entities purchase at both (a) the 340B price for 340B-eligible patients and (b) a non-340B price for ineligible patients (e.g., Medicaid carve-out).
- Covered entities (and their TPAs) choose to identify eligible 340B patients well after a dispense to such patient has occurred, including sometimes months after a dispense has occurred.
- There are no consistent, minimum standards or documentation requirements currently being enforced to ensure appropriate, transparent 340B patient identification.
- 340B-covered entities often utilize commercial contract pharmacies,⁷¹ outsourced dispensaries to patients of the covered entity made whole via replenishment.
- Covered entities and commercial contract pharmacies resist providing transparency and data to confirm 340B patient eligibility.
- Only some 340B covered entity pharmacy fills are to 340B-eligible patients, only some 340B covered entity pharmacy fills are to MFP-eligible patients, and those populations only sometimes overlap.

It will therefore be necessary for CMS to coordinate with the Health Resources and Services Administration (“HRSA”) to develop a mechanism to address these varied complexities.

In addition to these MFP-related concerns, a much larger issue exists around 340B patient eligibility when drugs are dispensed through contract pharmacies. Manufacturers do not have adequate insight into which prescriptions are designated as 340B-eligible by a covered entity and why. HRSA’s failure to enforce the 340B patient definition means that some pharmacies may claim 340B eligibility for prescriptions associated with patients who were treated at the covered entity at some point in the past, regardless of whether the prescription was written by a covered entity provider. Covered entity software vendors called “third party administrators” review contract pharmacy dispensing data in an effort to identify prescriptions associated with “patients of the covered entity;” however, this is defined at each covered entity. These software programs can even make strategic financial decisions and choose not to designate prescriptions as 340B-eligible if they are not sufficiently profitable. In many instances, multiple covered entities will claim 340B eligibility for the same prescription, leaving the manufacturer to pay a 340B chargeback multiple times for the same dispensed unit. These 340B program deficiencies, left unaddressed, will hinder the proper administration of the MFP.

CMS’s Guidance suggests that it may not yet be fully aware of the complexities of, or potential for ambiguity associated with, covered entities identifying 340B-eligible patients. Failure to appreciate and address these complexities could result in covered entities receiving both the MFP and a 340B discount for the same patient in violation of the IRA’s express requirements. CMS coordination with HRSA should focus on key areas that reduce the risk of duplicative

⁷¹ The 340B statute does not authorize the use of contract pharmacies and their use by 340B-covered entities raises serious concerns that drugs subject to 340B pricing are being diverted to non-patients or subjected to unlawful duplicate discounts. In light of these abuses, it is important that CMS put in place proper mechanisms, as described herein, to enforce the IRA’s non-duplication requirements and to ensure that covered entities receive only either the 340B price (if the patient is 340B eligible) or the MFP price (if the patient is MFP-eligible”), but not both.

discounts, including: (1) requiring that the identification of 340B-eligible patients and MFP-eligible patients must occur and be documented at the time of dispense; (2) establishing clear minimum documentation requirements for covered entities to support the identification of a 340B-eligible patient; and (3) requiring 340B discounts be paid as a rebate (as is currently the case with ADAPs) conditioned on the provision of adequate data to allow manufacturers to confirm the appropriateness of the discount and avoid duplicative MFP and 340B discounts.

VI. Conclusion

AbbVie strives to ensure that continued innovation and patient interests are upheld through the implementation of the IRA. Therefore, we urge CMS to comply with required notice-and-comment rulemaking procedures, allow for adequate public input, and respond meaningfully to requests, objections, and other feedback through this implementation process.

AbbVie appreciates this opportunity to provide input on this Guidance. If you have any questions, please feel free to contact Ashley Flint, Director, U.S. Policy & Analytics, at ashley.flint@abbvie.com.

Sincerely,

Hayden Kennedy

Hayden Kennedy
Vice President, Global Policy & U.S. Access Strategies
On behalf of AbbVie Inc.



April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Boulevard
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Submitted by email to IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of
Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026,
and Solicitation of Comments

Dear Director Seshamani:

The Academy of Managed Care Pharmacy (AMCP) thanks the Centers for Medicare & Medicaid Services (CMS) for the opportunity to provide comments in response to the above captioned guidance (the “Guidance”) setting forth CMS’ proposed policies for implementing the Medicare Drug Price Negotiation Program (Negotiation Program) for initial price applicability year 2026.

AMCP is the nation’s leading professional association dedicated to increasing patient access to affordable medicines, improving health outcomes, and ensuring the wise use of healthcare dollars. Through evidence and value-based strategies and practices, AMCP’s nearly 8,000 pharmacists, physicians, nurses, and other practitioners manage medication therapies for the 270 million Americans served by health plans, pharmacy benefit management firms, emerging care models, and government health programs.

Our comments are addressed below in the order in which they appear in the Guidance.

Section 30.3.1

The manufacturer of a biosimilar biological product (Biosimilar) may request, prior to the selected drug publication date, a delay in the inclusion of a negotiation-eligible drug that includes the reference product for the Biosimilar on the selected drug list. AMCP urges CMS to consider how to mitigate potential unintended consequences such as possible barriers to entry for new biosimilars and market forces that may exert upward pressure on prices.

Section 40.4 – Providing Access to the MFP.

In the guidance, CMS proposes to define “providing access to the MFP” to mean that the amount paid by the dispensing entity for the selected drug is no greater than the maximum fair price (MFP). To accomplish this, CMS proposes to require that the entity that holds the New

Drug Application(s) or Biologics License Application(s) for the selected drug (Primary Manufacturer) provide access to the MFP to dispensers (including pharmacies) in one of two ways: (1) by ensuring the price paid by the dispensing entity is no greater than MFP; or (2) by providing retrospective reimbursement for the difference between the dispensing entity's acquisition cost and the MFP. CMS thus intends to allow access to MFP by dispensers either at the point-of-sale or through the provision of retrospective reimbursement for the difference. Primary Manufacturers would be required to ensure that dispensers are reimbursed the difference between their acquisition cost and the MFP within 14 days.

AMCP believes it will be critical for dispensers, including pharmacies, to have access to MFP pricing at the point-of-sale. Existing supply chains do not generally contemplate payment directly from the manufacturer to the dispensing entity, nor are wholesalers and specialty distributors (who supply drugs to pharmacies) under any obligation to comply with the requirements to offer MFP. Fortunately, there is strong precedent and a clear model for facilitating manufacturer price concessions at the point-of-sale, already built into the existing Medicare Part D program. Under the Coverage Gap Discount Program (CGDP), CMS utilizes a third-party administrator (TPA) to aggregate Part D data, distribute invoices to manufacturers, and reimburse Part D plans for advancing access to the manufacturer discount at the point-of-sale. This existing framework for the CGDP (which CMS has indicated will be largely carried over with the transition to the new Manufacturer Discount Program (MDP) in January 2025) is the most effective approach to facilitate access to the MFP at the point-of-sale, and would fulfill the agency's policy goal of ensuring that stakeholders receive the full benefit of the MFP at the time of dispensing an MFP-eligible drug.

AMCP encourages CMS to explicitly recognize the roles of Part D plan sponsors and pharmacy benefit managers (PBMs) in being able to facilitate access to MFP prices at the point-of-sale through the existing CGDP framework or a framework modeled on this program.

Section 50.1. Manufacturer-Specific Data.

Section 1194(e) of the IRA directs CMS, for purposes of negotiating the MFP of a selected drug with the Primary Manufacturer, to consider certain factors, as applicable to the selected drug, as the basis for determining its offer. These factors are required to be reported by the Primary Manufacturer and include research and development (R&D) costs; current unit costs of production and distribution; prior Federal financial support for novel therapeutic discovery and development; data on pending and approved patent applications; exclusivities recognized by the FDA and FDA applications and approvals; and market data and revenue and sales volume data in the United States. As described in Appendix C of the Guidance, CMS is adopting a number of definitions to guide its data collection efforts. On March 21, 2023, CMS announced in the Federal Register an Information Collection Request (ICR) Form, as required by the Paperwork Reduction Act (PRA), for Negotiation Data Elements under Sections 11001 and 11002 of the IRA. AMCP intends to separately comment on this ICR request.

Overall, AMCP believes the definitions in Appendix C are comprehensive and clear but that some definitions may need to be fine-tuned over time as experience with the program brings additional context. For example, the definition of "global, total lifetime net revenue for the selected drug" may be more of an administrative lift than necessary if subtracting the "discounts, chargebacks, rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, other price

concessions or similar benefits” turns out not to be particularly impactful against overall global R&D costs and global revenue.

Section 50.2. Evidence About Therapeutic Alternatives for the Selected Drug.

The IRA requires CMS to consider “evidence about therapeutic alternatives” for purposes of negotiating an MFP for the selected drug. The factors on therapeutic alternatives CMS must consider include the extent to which the selected drug represents a therapeutic advance and the extent to which the selected drug and the therapeutic alternatives address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy. CMS must also consider the FDA-approved prescribing information for the selected drug and therapeutic alternatives, and evidence on the comparative effectiveness of the selected drug and its therapeutic alternatives.

AMCP’s members are at the forefront of evaluating therapeutic alternatives through our role on Pharmacy & Therapeutic Committee where we design value-based, patient-focused formularies built around scientific evidence. This collective experience in value-based formulary design leads us to support CMS’ reliance on therapeutic alternatives as an important factor for negotiating an MFP for a selected drug while urging caution about the potential for unexpected consequences. AMCP urges caution that the comparison with the therapeutic alternative may exert unanticipated market pressures, potentially increasing the comparator’s price. AMCP also believes that CMS should consider safety and efficacy of the selected drug versus the therapeutic alternative.

AMCP supports CMS’ approach to aligning the value of selected drugs with meaningful therapeutic alternatives. In the guidance, CMS states that it intends to consider evidence about therapeutic alternatives submitted by members of the public, including manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested parties. AMCP appreciates an approach that relies on public feedback and stakeholder solicitations to arrive at appropriate therapeutic alternatives, given the complexities involved in evaluating clinical evidence and placing drugs on formularies. Therapeutic alternatives can serve as a useful benchmark and guide the decision-making process, helping to meet medical needs and assuring clinical effectiveness. CMS’ robust approach to assessing therapeutic alternatives, including considering a variety of patient-centered factors, supports value for patients.

Section 60.3. Methodology for Developing an Initial Offer.

In developing an initial offer, CMS intends to identify therapeutic alternatives, if any, for the selected drug; use the Part D net price for the therapeutic alternatives to determine a starting point for developing an initial offer; evaluate the clinical benefit of the selected drug (including compared to its therapeutic alternatives) for the purposes of adjusting the starting point using the negotiation factors, resulting in the preliminary price; and further adjust the preliminary price by the negotiation factors to determine the initial offer price.

AMCP supports CMS’ approach to relying on the net price of therapeutic alternatives as the starting point for negotiating for the selected drug. AMCP agrees with CMS’ plan to use the net prices from Part D as this is a more accurate reflection of revenue than the listed price. This approach mirrors the approach used by many payers when developing formularies, including an assessment of the value of the drug, performed after the clinical evaluation, by evaluating the net cost, market share, and drug utilization trends of clinically similar medications.

As CMS continues to develop the Negotiation Program, AMCP urges the agency to ensure that there are no unintended consequences that could undermine existing market-based negotiations. While CMS intends to address the renegotiation process in greater detail in future guidance, it is important to note that one of the limited circumstances in which the statute allows for renegotiation is for a “material change” to the manufacturer-specific negotiation factors, which CMS is proposing to define in this Guidance. In particular, CMS is proposing in Appendix C to define “market data and revenue and sales volume data” to include the average net unit price of the selected drug for Part D plan sponsors. This raises the concern that a manufacturer negotiating discounts or rebates in excess of the MFP could be risking the prospect of renegotiation, unless CMS clarifies in future guidance that such negotiations *will not* suffice to qualify as a “material change” to the manufacturer-specific negotiation factor that would require a selected drug to undergo renegotiation. In the absence of such clarity, AMCP is concerned that market-based negotiations will be hampered, essentially resulting in the MFP becoming a ceiling for any future negotiations.

Section 70. Removal from the Selected Drug List Before or During Negotiation, or After an MFP is in Effect.

Under the IRA a selected drug will no longer be subject to the negotiation process and will cease to be a selected drug, subject to the timeline and situations discussed below, if CMS determines the FDA has approved a generic drug under section 505(j) of the FD&C Act that identifies as its reference listed drug a product that is included in the selected drug, or the FDA has licensed a biosimilar biological product under section 351(k) of the PHS Act that identifies as its reference product a product that is included in the selected drug; and the generic drug or biosimilar biological product, as applicable, is marketed pursuant to such approval or licensure.

Biosimilar and generic competition are critical to lowering the overall cost of therapies and enhancing formulary competition. As a result, CMS should take all steps necessary to remove impediments to market-based negotiations to ensure that “robust and meaningful” competition from generic or biosimilar entrants is encouraged. In particular, expeditious removal of a selected drug when removal criteria are met will be essential to allow Plan D sponsors and PBMs to fulfill their role of promoting substitution of generics and biosimilars as lowest net cost products, where applicable. At a time when health care expenditures are escalating at alarming rates, greater access to safe and effective biosimilars and generics can aid in reducing prescription drug expenditures for patients and payers.

Section 110. Part D Formulary Inclusion of Selected Drugs.

As noted in the Guidance, CMS intends to require Medicare Part D plans to include in their Part D formularies “each covered Part D drug that is a selected drug” during 2026 and all subsequent years for which the MFP of the selected drug is in effect. While AMCP has not provided comment on Section 30 of this Guidance (as the agency noted it is not open for comment), it is important to note that the proposed broad interpretation of qualifying single source drugs (QSSD) raises concerns about formulary inclusion of selected drugs. Most notably, AMCP notes that CMS’ broad approach to defining QSSDs may lead to an increased number of unique marketed products subject to MFP each year. QSSD is defined to include all dosage forms and strengths of the drug with the same active moiety, meaning potentially dozens of drugs, including multiple NDAs, would fall under the same QSSD definition. We are particularly concerned about drugs with the same active ingredient but different modes of administration. There may be substantial cost variation among different modes of

administration. There is a risk that the MFP could be set too low, causing potential issues for patient access. CMS should also consider what could happen if the drug's dosage forms overlap between Part B (for example, infused dose form) versus Part D (oral dose form). It is therefore critical that CMS clarify that the agency will not require formularies to include every dose form and strength of the QSSD, including new formulations. While such an interpretation is clearly not supported by the statute and would fundamentally undermine value-based formulary design, clarity on this issue is critical to avoid disrupting formulary negotiations.

An approach that requires formulary coverage of all dosage forms and strength of the QSSD, including new formulations, is out of step with current practice and would harm the market-based negotiations that currently underly the Part D program. Current practice involves evaluation of the indications and differences in safety, efficacy, and cost. If there are differences based upon formulation, then step requirements or medical justification are often considered for a specific dosage form. There can often be significant cost differences between a tablet or capsule formulation, an injectable, and an oral solution for any given product. There might also be reasons (e.g., swallowing disorders, G- or J- tubes, advanced conditions that impact swallowing) that justify the specialized or more costly dosage form, but these could be addressed by medical necessity review. AMCP recommends that plans be required to cover at least one dosage form, with an option for members and/or providers to request an alternative medically necessary dosage form. This would allow health plans to cover medically necessary dosage forms without the potential burden and increased costs of covering all dosage forms regardless of medical necessity.

Finally, AMCP encourages CMS to provide clarity that the formulary inclusion requirement does not otherwise disrupt existing formulary management tools, including value-based tools such as utilization management (UM) that are used to ensure that drugs are provided in the safest and most cost-efficient manner. CMS should continue to allow Part D plans the flexibility to implement UM edits on selected drugs to ensure safety and appropriate utilization. The initial guidance notes that the negotiated drugs must be on formularies but does not require a specific tier. AMCP supports this flexibility for plans when building their formularies.

Conclusion

AMCP appreciates your consideration of the concerns outlined above and looks forward to continuing work on these issues with CMS. If you have any questions regarding AMCP's comments or would like further information, please contact AMCP's Director of Regulatory Affairs, Geni Tunstall, at etunstall@amcp.org or (703) 705-9358.

Sincerely,



Susan A. Cantrell, MHL, RPh, CAE
Chief Executive Officer



VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

11 April 2023

Dear Administrator Brooks-LaSure,

Re: Medicare Drug Price Negotiation Program Guidance

Achilles Therapeutics appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

We are a clinical-stage biopharmaceutical company developing precision T cell therapies to treat solid tumor cancers including advanced non-small cell lung cancer (NSCLC) and recurrent or metastatic melanoma. The therapy we are developing, which uses cutting edge technology to find personalized neoantigen targets in each patient, could become the first genomic cell therapy.

While our investigational product is a biologic, we can empathize with our peers at other companies who are working on small molecules that the IRA, in our view, just made far less attractive to investors that provide the required capital for pre-revenue, drug developers. Without this capital, innovative early-stage companies like ours simply cannot afford to create these potentially lifesaving medicines for the patients who need them.

We are fortunate that biologics have retained 13 years of market-based pricing before having their price impacted by Medicare negotiation (which also spills over into Medicaid) and would urge CMS to only reduce the prices of small molecule drugs during the 9-13 year period as little as required by IRA. Wherever it may be possible to interpret the IRA in such a way as to exempt a small molecule from the IRA, we hope CMS will do so.

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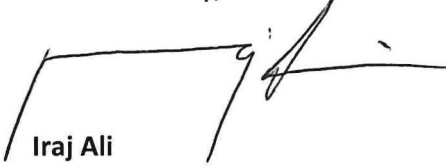
Achilles Therapeutics plc is a public limited company registered in England and Wales with registered number 13027460. Registered Office: 245 Hammersmith Road, London W6 8PW.



We believe that encouraging investment in both small molecule and biologics companies will ultimately benefit patients who currently have no or limited treatment options.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. Please contact Lee Stern, our VP of Investor Relations, by telephone at (917) 312-5998 or by e-mail at l.stern@achillestx.com if you have any questions regarding our comments.

Yours faithfully,



Iraj Ali
CEO

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Achilles Therapeutics plc is a public limited company registered in England and Wales with registered number 13027460. Registered Office: 245 Hammersmith Road, London W6 8PW.

April 10, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Aerovate Therapeutics appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance). I understand that CMS is not allowing comments on Section 30 of the IRA which outlines the selection process for drugs in the first year of the program, but I am providing the comments that would have been made if allowed.

Aerovate Therapeutics is developing a small molecule for the potential treatment of Pulmonary Arterial Hypertension (PAH), a fatal disease for which we have Orphan designation. Aerovate's drug candidate is AV-101, a novel **inhaled formulation** of the generic **oral drug imatinib**. Oral imatinib is approved for treating leukemia and other rare forms of cancer. Oral imatinib was also studied in a global clinical trial in patients with PAH, and although oral imatinib was highly effective in the PAH trial, systemic administration of oral imatinib resulted in serious adverse events and development was discontinued. Oral imatinib was not approved for the treatment of PAH patients because of the unacceptable safety profile of oral imatinib in PAH patients.

Aerovate was founded based on the invention of a novel (i.e., patent-protected) inhaled formulation of imatinib that targets the lung directly, and is therefore administered in doses that are 65%-80% lower than the dose of oral imatinib that was shown to be highly effective but unacceptably toxic in PAH patients. We believe a lower dose of inhaled imatinib could provide a novel, effective treatment for patients without the toxicity of oral imatinib. Although generic imatinib exists, it cannot be safely used to treat PAH, but we are concerned that AV-101 could be categorized with oral imatinib based on the active moiety.

By making Aerovate's AV-101 potentially eligible for price negotiation at nine years, CMS's guidance in Section 30 could undermine continued investment in clinical development, and pose a significant threat to a novel, potentially life-saving Orphan drug. If CMS were to cite generic imatinib to invalidate the ODD exemption for AV-101, then CMS ought to include generic imatinib to conclude AV-101 isn't a single-source drug eligible for negotiation. Thank you very much.

Sincerely,

A handwritten signature in blue ink that reads "Timothy Noyes".

Timothy Noyes
Chief Executive Officer
Aerovate Therapeutics, Inc.
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April 13, 2023

Dr. Meena Seshamani, Director, Center for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

RE: Medicare Drug Price Negotiation Program Guidance

Submitted via email to: IRAREbateandNegotiation@cms.hhs.gov

Dear Dr. Seshamani:

Every American deserves access to affordable prescription drugs, and with that commitment in mind, AHIP¹ appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program Guidance issued March 15, 2023 (the Guidance). The Guidance is focused on the process by which the Centers for Medicare & Medicaid Services (CMS) will negotiate Maximum Fair Prices (MFP) with drug manufacturers for a limited number of single-source Medicare Part D drugs for 2026, pursuant to sections 11001 and 11002 of the Inflation Reduction Act (IRA). The Guidance is also of interest to our members, many of which offer Part D coverage, given its potential implications for their delivery of Part D benefits and other types of coverage.

As advocates for Americans that negotiate lower drug prices for patients and consumers, health insurance providers have provided seniors and people with disabilities with robust access to prescription drugs through Part D coverage and kept premiums steady since the program's inception. Health insurance providers add tremendous value by negotiating lower costs with drug manufacturers and pharmacies, leveraging proven and effective cost-management and negotiating tools. To support these efforts in Part D and for other types of coverage, AHIP has consistently supported market-based solutions that deliver real competition; remove barriers to full and fair negotiation; create more consumer choice; and ensure open and honest drug prices for patients, consumers, employers, and government payers. Our policy recommendations have included:

- Using evidence-based criteria for comparing the value of treatment options, along with expanding flexibility in using other formulary management tools for high-cost drugs for which rebates are often limited or unavailable (e.g., for protected class drugs and drugs with no therapeutic competition).
- Increasing transparency in how drug prices are set and increased, which would help to mitigate anticompetitive pricing practices, allow patients to make informed decisions, and allow Americans to recognize when drug companies have been hiking prices as well as when competition is working to keep drugs affordable.
- Taking various steps such as improved clinician and patient education and product approvals to create a more robust and competitive marketplace for biosimilars as affordable alternatives to expensive branded biologics.

¹ AHIP is the national association whose members provide health care coverage, services, and solutions to hundreds of millions of Americans every day. We are committed to market-based solutions and public-private partnerships that make health care better and coverage more affordable and accessible for everyone. Visit www.ahip.org to learn how working together, we are Guiding Greater Health.

- Preventing brand-name drug manufacturers from using risk evaluation and mitigation strategies (REMS) and other egregious drug company practices to block competition from generic drug makers.

Our comments below are focused on interpretive elements in the Guidance that could affect these key objectives regarding enhanced competition, choice, and affordability in Part D and other programs.

Section 30 – Identification of Selected Drugs for Initial Price Applicability Year 2026:

AHIP Comments: AHIP understands that CMS is not accepting comments on the criteria for identifying and selecting Part D drugs for Initial Price Applicability Year 2026, given the practical challenges of meeting implementation timelines.² However, it is important for CMS as a matter of course to make important guidance documents available for public comment to the greatest extent possible, regardless of statutory authority that exempts any particular guidance from notice-and-comment processes. It is critical that stakeholders have an opportunity to provide feedback notwithstanding CMS’ view that a particular piece of guidance may be “unnecessary” or that feedback is “contrary to the public interest.” Meaningful comment from the public is fundamental to ensuring that the agency can adequately assess the costs and benefits of particular policies and consider alternatives. Accordingly, we urge CMS to solicit comments on section 30 for future price applicability years, and to commit to notice-and-comment processes for future guidance documents relating to the IRA.

Section 40.2.1 – Confidentiality of Proprietary Information:

Section 1193(c) of the Social Security Act, as added under the IRA, provides that information submitted by a manufacturer that is proprietary information (as determined by CMS) shall be used only by CMS or disclosed to the Comptroller General of the United States for purposes of carrying out the IRA. Guidance Section 40.2.1 describes CMS’ proposed confidentiality policies for proprietary manufacturer-specific data (detailed in Appendix C of guidance) that will be collected to inform negotiations, and for certain other aspects of that process.

In general, CMS states that it will treat as proprietary information and not publicly disclose any commercial or financial information submitted by manufacturers that cannot be found publicly. CMS specifies that research and development costs and recoupment, unit costs of production and distribution, pending patent applications, and market data and revenue and sales volume data will be treated as proprietary unless publicly available. CMS also specifies that data on prior Federal funding and approved patent applications, exclusivities, and applications and approvals under section 505(c) of the FD&C Act or section 351(a) of the PHS Act will be treated as non-proprietary because CMS believes these data are available publicly.

CMS further states that it will not publish proprietary information as part of public documents otherwise discussing the MFP, including in the explanation for a selected drug’s MFP that CMS is required to publish under the IRA. CMS indicates such public documents will include only “high-level” comments about data submitted. As a specific example, the guidance notes CMS could indicate that for a particular MFP a manufacturer will have “recouped its research and development costs.”

² However, CMS is accepting comments in response to a separately-issued information collection request for data relating to implementation of an exception for small biotech drugs.

AHIP Comments: AHIP supports protection for non-public commercial, financial, and other non-public proprietary information that may be collected under the IRA. Government confidentiality policies that protect proprietary information that may be collected for purposes of implementing and overseeing programs like Medicare Part D (such as in exemptions from disclosure under the Freedom of Information Act) advance important public policy goals, including safeguarding private entities from the competitive disadvantages that could result from disclosure.

We note that in some circumstances, a government policy that provides for release of “high level” government comments about proprietary data collected for purposes of implementing or overseeing programs could also have anti-competitive effects, depending on the particular facts and circumstances of the comments. We recognize CMS is adopting this policy under the unique circumstances of the IRA, which requires CMS to publish an explanation for each MFP with respect to the factors that CMS considered, including manufacturer-specific data, while it also requires that CMS keep proprietary information confidential. We urge CMS to limit this policy to the IRA and continue to provide strong protections to proprietary data otherwise collected under Part D.

Section 40.2.2 – Data Use Provisions and Limitations:

CMS will prohibit manufacturer disclosure to the public of any information contained in CMS’ initial or subsequent offers, including ceiling prices, etc., nor use such information “. . . for any purposes other than the Medicare Drug Price Negotiation Program, except as may be required by applicable state or federal law.”

AHIP Comments: We agree that manufacturer disclosure or use of information in connection with the negotiation process could be problematic. Especially concerning would be the potential opportunities presented for manufacturers to selectively release information that could be presented out of context and used to manipulate negotiations in Part D or other programs, thereby increasing costs to patients, employers, and taxpayers. As noted above, AHIP supports market-based solutions that include full and fair negotiations to enhance affordability and choice for Americans. Accordingly, to avoid potential anti-competitive impacts for other drugs within Part D and for other programs, we agree that CMS should adopt policies relating to confidentiality of negotiations that are as consistent as possible with private sector negotiation processes.

Section 50 – Negotiation Factors:

For purposes of negotiating the MFP for a selected drug, in addition to considering manufacturer-specific data, Section 1194(e)(2) of the Social Security Act added by the IRA provides that CMS must evaluate evidence about therapeutic alternatives. Under the Guidance, CMS will use evidence about therapeutic alternatives submitted by members of the public such as “. . . manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested parties.”

AHIP Comments: We appreciate CMS’ recognition that parties aside from drug manufacturers have valuable perspectives and unique information on evidence about therapeutic alternatives, and we support CMS’ proposal to allow submission of this information from non-manufacturer parties. Health insurance providers and their contracted pharmacy benefit managers (PBMs) have a core role in the American health care system in providing safe and affordable access to prescription drugs. In fulfilling this role, they use evidence-based reviews of clinical data, including therapeutic alternatives, in negotiations with drug manufacturers and in establishing benefit designs and formulary management tools to create a cost-effective system that encourages competition and the use of high-value drugs. Given this role and

expertise and the potential for negotiations for prices of selected drugs in Part D to have broader implications within the Part D program and beyond, we encourage CMS to specifically cite health insurance providers and PBMs as another group of “interested parties” permitted to submit evidence about therapeutic alternatives.

Section 50.2 – Evidence About Therapeutic Alternatives for the Selected Drug:

Section 1194(e)(2) of the Social Security Act, as added by the IRA, provides for CMS to use the following if available in considering therapeutic alternatives:

- The extent a selected drug is a “therapeutic advance” compared to existing Rx treatments;
- FDA-approved prescribing information and its therapeutic alternatives;
- Comparative effectiveness of the selected drug and therapeutic alternatives, including effects on specific populations, such as individuals with disabilities, the elderly, the terminally ill, children, and other patient populations; and
- Whether the selected drug and available alternatives address needs unmet by available therapies.

The Guidance indicates that in addition to considering information submitted by manufacturers and the public, CMS will review existing literature and “real-world” evidence, conduct internal analytics, and consult subject matter and clinical experts. The Guidance describes key metrics to be used in assessing the literature. The Guidance also indicates that CMS will prioritize research specifically designed to focus on Medicare populations - individuals with qualifying disabilities, patients with ESRD, and Medicare-aged populations - over studies for which these populations were not the primary focus.

The Guidance also notes the prohibition in the IRA on use of comparative clinical effectiveness research that treats extending the lives of individuals who are elderly, disabled, or terminally ill as of lower value than those of individuals without such status. CMS specifies that for purposes of the negotiation process, the agency will not take into account information submitted by the public or otherwise considered by CMS that uses quality adjusted life years (QALYs). The agency solicits comments on other metrics that should be excluded from consideration.

AHIP Comments: Concerns and prohibitions on the use of QALYs have generated alternative comparative effectiveness measures that do not differently value life extension based on the enumerated characteristics. These measures, including the equal-value life year gained (evLYG), health years in total (HYT), and generalized risk adjusted QALY (GRA-QALY), are important metrics for CMS to employ when meeting the statutory requirement to assess the comparative effectiveness of the negotiation-eligible drug relative to therapeutic alternatives. Comparative effectiveness metrics serve to expand access by helping to reduce the high prices caused by drug manufacturers’ long-standing practice of pricing drugs far above their value. Further, Part D formulary requirements ensure continued access to drugs, including those for which comparative effectiveness metrics are applied. We strongly urge CMS to affirmatively recognize that non-QALY metrics are appropriate, and indeed required, elements of price negotiation.

Section 90.4 – Monitoring for Bona Fide Marketing of Generic or Biosimilar Product:

Under the IRA, a selected drug is no longer subject to negotiation if CMS determines: (1) the FDA has approved a generic drug or biosimilar for which the selected drug is a reference product, and (2) the generic drug or biosimilar biological product is marketed pursuant to such approval or licensure. CMS provides examples of monitoring that include whether the drug or biosimilar product is regularly and

consistently available for purchase through the pharmaceutical supply chain and whether it is available for purchase by community retail pharmacies in sufficient quantities from their wholesale suppliers. CMS also intends to analyze the share of generic drug or biosimilar product units identified in Part D Prescription Drug Event (PDE) data as a percentage of total units of Part D expenditure.

AHIP Comments: Drug manufacturers repeatedly use myriad schemes and techniques to limit generic competition. For example, the manufacturer Celgene recently entered into an agreement to allow extremely limited generic competition for the drug Revlimid (lenalidomide). Under this agreement, from March 2022 through December 2026, one sole generic manufacturer would be allowed to market generic lenalidomide under the condition that total sales of the generic drug remain less than 10 percent of total Revlimid/lenalidomide sales.³ This arrangement is an example of how manufacturers engage in anticompetitive activities to forestall the price benefits of generic competition. CMS should consider taking steps to monitor and shine a light on such arrangements. Schemes designed to avoid bona fide marketing of generic or biosimilar products not only affect the negotiation status of a selected drug, but they reduce competition and limit affordability of products for patients and other stakeholders more broadly in Part D and other programs.

Section 110 – Part D Formulary Inclusion of Selected Drugs:

The IRA requires Part D plans to include each covered Part D drug that is a selected drug on Part D formularies during Contract Year (CY) 2026 and all subsequent years for which the MFP of the selected drug is in effect during the price applicability period. This section in the Guidance reiterates those requirements for implementation.

AHIP Comments: The IRA does not specify how selected drugs are required to be included on Part D formularies. Accordingly, nothing in the IRA should prohibit Part D plans from using formulary designs and formulary management activities with respect to selected drugs based on input from Pharmacy and Therapeutics (P&T) committees, scientific evidence, and pharmacoeconomic considerations to support appropriate, safe, and cost-effective access to the extent permitted for other drug therapies.

We encourage CMS to reiterate these plan flexibilities. We also encourage CMS to clarify when the formulary inclusion requirement does not apply. One example would be when a selected drug ultimately does not become subject to an MFP due to the introduction of a generic or biosimilar competitor after the drug selection. Another example is the ability specified in the IRA to remove a selected drug from the formulary when a therapeutically equivalent generic drug becomes available to the extent permitted under Part D regulations. CMS should further clarify the availability of other Part D plan flexibilities (such as changing a brand name drug's preferred or tiered cost-sharing) when a generic drug or biosimilar becomes available.

In addition, the Guidance (in Section 60.6) reiterates the statutory requirement that CMS publish, by September 1, 2024, the MFP for each selected drug for CY 2026. Given the formulary inclusion requirement and other provisions (e.g., a Part D plan's negotiated price for a selected drug cannot exceed the MFP plus any dispensing fee), it is critical that CMS meet this publication deadline so Part D plans can appropriately operationalize these provisions and incorporate them into pharmacy negotiations and bid development for 2026.

³ <https://ir.celgene.com/press-releases-archive/press-release-details/2019/Celgene-Settles-US-REVLIMID-Patent-Litigation-with-Alvogen/default.aspx>

Again, AHIP appreciates the opportunity to offer comments on the Medicare Prescription Drug Price Negotiation Program initial memorandum. We also urge CMS to carefully consider options to minimize potential disruptive impacts from additional operational changes to the program's enrollees and other stakeholders, such as changes to pharmacy acquisition and reimbursement processes that may adversely affect long-established supply-chain operations. We look forward to continuing to work with CMS to achieve the shared goal of lower drug prices and more affordable access for Medicare-eligible Americans. Please contact me if additional information would be helpful or if you have questions about the issues raised in this letter. I can be reached at (202) 778-3256 or mhamelburg@ahip.org.

Sincerely,

A handwritten signature in black ink, appearing to read 'mhamelburg', written in a cursive style.

Mark Hamelburg
Senior Vice President, Federal Programs

April 14, 2023

Chiquita Brooks-LaSure
Administrator
Center for Medicare
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Sent Electronically to IRAREbateandNegotiation@cms.hhs.gov

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Brooks-LaSure:

We are leaders in advancing education, advocacy, and research for those impacted by autoimmune and autoinflammatory arthritis (AiArthritis) diseases through peer-led guidance, collaboration, and resources that are driven by patient-identified issues and patient-infused solutions. As we are led by patients we understand the importance of ensuring better health outcomes and lower costs for patients, particularly those with chronic, degenerative diseases like Psoriatic Arthritis, Rheumatoid Arthritis, Lupus, Spondyloarthritis, and over a dozen other AiArthritis Diseases.

We thank the Centers for Medicare & Medicaid Services (CMS) for the opportunity to submit comments on the *Medicare Drug Price Negotiation Program Initial Guidance* for the initial price applicability year of 2026. We understand that this step was not explicitly required in the *Inflation Reduction Act* (IRA) and it is appreciated by patient groups. The Maximum Fair Price (MFP) provisions within the IRA provide CMS with significant new authority to reduce drug prices for Medicare beneficiaries. As your guidance recognized, the MFP provisions of the law also include requirements to protect patients and support patient-centered action. With this new authority, CMS has the opportunity to advance the crucial goal of ensuring better outcomes and reducing costs for patients throughout the implementation of the Medicare Drug Price Negotiation Program. It is imperative that CMS center its decisions around patients and key components that may impact their access to optimal care.

We believe AiArthritis and CMS aim to achieve better health outcomes for patients. While there are several areas we could address, the following considerations focus on key points considerate of heterogeneous diseases where one-size-fits-all treatments do not exist. We respectfully suggest CMS refines its negotiation process to consider: 1) The welfare of patients must be in the forefront of the implementation, and their input should be considered 2) There must be incentives for innovation by the

pharmaceutical industry 3) Transparency must be prioritized 4) The use of the QALY from any secondary source should be justified in any price negotiation 5) Precision Medicine must be considered when research demonstrates a trial-and-error approach can lead to worse outcomes and elevated healthcare costs.

1. **Patients and Patient Organizations must be included at every step along the way.** We are an organization whose leadership is comprised entirely of patients with AiArthritis disease, thus we bridge broad patient voice representation with actual patient voice perspectives. As such we look forward to being more involved with providing feedback as CMS continues forward with this process. We are dedicated to working with other patients and Patient Organizations who represent the community voice, as well as all other stakeholders as CMS undertakes drug price negotiation. **We ask that you provide meaningful opportunities for all of us to give continuous feedback during all steps of the process - especially with regard to our viewpoints on value, preferred outcomes, updated research, societal benefits, and unmet need.**
2. **Access to innovative treatments is vital for those with rare disease.** 95% of all rare diseases have no FDA approved treatment. Thus, drug price negotiations should not disrupt innovation and patient access to the best therapies for their unique needs. In addition to all of our diseases being heterogeneous, some are also rare. We appreciate that the IRA included a limited exception for orphan drugs (drugs that treat only one rare disease) from negotiation. However, we are concerned that this will disincentivize pharmaceutical companies from conducting research into treatment for other diseases for fear that the drug will be subject to price negotiation. Failure to appropriately categorize these medications would stymie research with regard to additional therapeutic options for orphan drugs. There must be incentives for the pharmaceutical industry to continue to innovate, otherwise those with rare disease will continue to be alienated. **We ask that CMS clarify that obtaining additional designations for a drug will not make that drug eligible for negotiation unless and until it is approved by the FDA for another disease.**
3. **Maintain transparency in drug price negotiations to ensure accountability, build public trust, realize cost savings, and achieve better outcomes for patients.** Accountability is essential to ensure that CMS is acting in the best interest of the public. Transparency during negotiations will demonstrate that CMS is dedicated to fair and unbiased decision-making. When the public and stakeholders are able to see how prices are determined, it will help drive innovation and competition, resulting in lower prices and more variability in medications. **We urge CMS to be sufficiently transparent so that all stakeholders are informed on its progress and can be assured that the negotiation process is fair and equitable.**
4. **We realize that while CMS has requested input on other measures that might be used as a substitute for the QALY, data generated from its past implementation is extensive.** So while we understand that the IRA prohibits CMS from using QALY metrics in the negotiation, there

are no provisions to limit secondary sources that incorporate QALY-related data in evaluations. Our rationale for concern lies in the restrictive nature of the QALY, which does not account for patient heterogeneity, disease progression, or other factors that are not considered in general population models. **When and if this occurs, we suggest CMS justify the incorporation of that data, CMS should also prioritize patient and patient organization viewpoints, clinical utility and effectiveness, societal benefits, and patient-centered health outcomes in all pricing considerations.**

- 5. Precision Medicine is considered as a viable and necessary component of disease management and improving healthcare costs.** Precision medicine can expedite diagnosis, accelerate matching patients to treatments that can help doctors identify and better treat aggressive disease, predict harmful side effects, and eliminate costly trial-and-error processes. For diseases like ours, where no two patients are alike, it provides hope that we can gain access to a treatment that may work the first time, rather than spend years trying and failing various options. It provides hope that remission is possible, as now most of us will remain on costly medications for the rest of our lives. Its impact will improve outcomes, decrease rates of disability, and produce cost savings to the healthcare system. However, since little is said regarding consideration of precision medicine in negotiations, we wanted to take this opportunity to express its importance. **We encourage CMS to consider precision medicine in its negotiations, especially as implementation methods may impact patient access to both new and existing treatments.**

As a patient-led organization focused on improving the lives of those impacted by autoimmune and autoinflammatory arthritis (AiArthritis) diseases, we urge CMS to consider these recommendations. Together we can achieve the crucial goal of ensuring better outcomes and reducing costs for patients. Thank you again for this opportunity and for considering what patients feel is most important.

Sincerely,



Lindsey Viscarra
Public Policy Manager



Tiffany Westrich-Robertson
Chief Executive Officer

BY ELECTRONIC SUBMISSION VIA IRAREBATEANDNEGOTIATION@CMS.HHS.GOV

April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health & Human Services
7500 Security Boulevard
Baltimore, MD 21244-1850

**RE: Medicare Drug Price Negotiation Program: Initial Memorandum,
Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price
Applicability Year 2026, and Solicitation of Comments**

Dear Deputy Administrator Seshamani,

Alexion, AstraZeneca Rare Disease (Alexion) appreciates the opportunity to comment in response to the above captioned guidance (the “Guidance”) setting forth the Centers for Medicare & Medicaid Services’ (CMS’) proposed policies for implementing the Medicare Drug Price Negotiation Program (Negotiation Program) for initial price applicability year (IPAY) 2026.

Alexion is the group within AstraZeneca focused on rare diseases. Our mission is to transform the lives of people affected by rare diseases through the development and delivery of innovative medicines as well as supportive technologies and health care services. For 30 years, patients and their caregivers have been at the center of everything we do, and our mission is driven by understanding who they are as unique individuals, not just their disease. Every day, we are inspired to think differently and follow the science to create better outcomes for them and their families.

Our pioneering legacy in rare diseases is rooted in being the first to translate the complex biology of the complement system into transformative medicines. We have delivered transformative medicines for people living with paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome, antiaquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (NMOSD), generalized myasthenia gravis (gMG), hypophosphatasia, and lysosomal acid lipase deficiency (LAL-D). Today, we continue to push the boundaries of science and deepen our understanding of rare diseases. This knowledge allows us to innovate and evolve into new areas where there is great unmet need and opportunity to help people fully live their best lives. We have provided comments regarding the Guidance in a section-by-section format, below. Our key areas of focus can be summarized as follows:

- **Alexion opposes CMS's “qualifying single source drug” (QSSD) definition as overly broad and not supported by the statute.** For both small-molecule drugs and large-molecule biological products, the statute unambiguously anchors the QSSD definition to the singular approval by the Food and Drug Administration (FDA) under which the product is marketed. The statute in no way authorizes CMS to convert the statute's focus on a

singular FDA approval to a definition that sweeps in products with multiple separate FDA approvals through the addition of an “active moiety/ingredient” test. As such, the term QSSD should be defined no more broadly than the NDA/BLA, which is the approval under which the product is originally marketed. CMS’s aggregate approach to defining QSSD may stymie innovation and limit patient access to new therapies that could improve their health outcomes.

- **Alexion appreciates CMS’s recognition of Congressional intent to exclude orphan drugs from the Negotiation Program, as well as CMS’s request for feedback about how to best preserve the orphan drug development pipeline. Unfortunately, the agency’s interpretation of the orphan drug exclusion is inconsistent with the statute, and we recommend that CMS exclude from inclusion in a QSSD any products marketed under a distinct NDA or BLA which are individually eligible for the orphan drug exclusion.** Specifically, because CMS is defining QSSD by reference to active ingredient/moiety, a single QSSD could include multiple drugs approved under separate NDAs/BLAs. Under CMS’s policy, an orphan drug approved under a new NDA/BLA would not fall within the scope of the orphan drug exclusion if it were aggregated into a broad QSSD with non-orphan products with the same active ingredient/moiety, which would discourage the development of orphan drugs and thus runs contrary to Congress’ decision to exclude orphan drugs from negotiation. However, the statute is clear that a QSSD cannot include a drug that would qualify for the orphan drug exclusion, and this approach preserves incentives to continue to develop orphan drugs and avoids arbitrarily failing to apply the orphan drug exclusion to qualifying drugs based solely on their aggregation into a QSSD with other non-qualifying drugs.
- **To preserve the incentive structure established by the Orphan Drug Act, Alexion also asks CMS to exclude from negotiation any product for which all indications, in the aggregate, treat fewer than 200,000 patients in the United States.** The express purpose of the ODA is to encourage the development of innovative pharmaceutical products to treat diseases and conditions with very small patient populations, defined by Congress as those affecting fewer than 200,000 persons in the United States. While the IRA includes an orphan drug exclusion, evincing a clear intent to preserve Congress’ longstanding support and incentives for drugs treating small patient populations, namely populations of fewer than 200,000 patients, CMS’ approach to implementing this exception fundamentally disrupts this purpose by leaving unprotected rare disease therapies that treat fewer than 200,000 patients even across multiple indications.
- **Alexion further urges CMS to support orphan drug development by clarifying that, in the context of an orphan drug, the 7- or 11-year period that must elapse before a drug can be considered for negotiation begins upon the date that the orphan drug exclusion no longer applies.** CMS should issue additional guidance to clarify that the orphan drug exclusion insulates a product from the IRA’s negotiation provisions for the entire duration the exclusion applies. Notably, the orphan drug exclusion constitutes a

threshold exclusion from the definition of a QSSD. It must follow from this structural placement that the 7- or 11-year pre-negotiation period that would otherwise apply to a QSSD is *tolled* until the first day after the orphan drug no longer meets the requirements of the orphan drug exclusion. This approach will better enable innovator companies to initially pursue orphan indications by initiating the pre-negotiation period only upon a subsequent approval for a distinct disease or condition.

- **Alexion urges CMS to take a holistic approach to considering a selected drug's clinical value.** While Alexion appreciates that CMS is required by statute to take into consideration certain factors in setting the maximum fair price (MFP) for a selected drug, we note that such factors are to be considered only “as applicable to the drug” and not all the statutory negotiation factors must be weighted equally. We recommend that CMS replace its proposed approach with one that accounts for the clinical value of a product using five core principles (outlined below). We also encourage CMS to implement an MFP methodology that provides the MFP ceiling price for products that either treat conditions with an unmet need or represent a significant therapeutic advance.
- **Alexion urges CMS to provide a more detailed framework regarding how the agency intends to consider therapeutic alternatives and evaluate comparative effectiveness, and to engage manufacturers on the shared objective of assessing a treatment’s clinical value.** There are numerous open questions that warrant CMS engaging the selected drug manufacturer regarding the methodology that the agency will use to evaluate therapeutic alternatives and assess comparative effectiveness.
- **Alexion supports CMS’s policy of not considering QALYs for purposes of the Negotiation Process, which is consistent with the plain statutory language of the IRA.** We similarly support the agency's scrutiny of any comparative effectiveness research that may rely on QALYs for its conclusions.

We describe each of these comments in greater detail, below.

I. Section 30: Identification of Selected Drugs for Initial Price Applicability Year 2026

Alexion understands that CMS has limited time to implement the Negotiation Program for IPAY 2026 and we acknowledge that CMS is issuing section 30 of the Guidance in final form without an opportunity to comment. However, Alexion is concerned that CMS is moving forward with policies that significantly reshape the way drugs are priced in the Medicare program without providing the public with the opportunity for comment, particularly because some of the policies described in section 30 appear to exceed the agency's statutory authority, and others pose significant policy or operational concerns that the agency may not have considered. Alexion is therefore submitting comments on section 30 and urges CMS to take these comments into account in the agency's implementation of the Negotiation Program going forward.

- A. CMS’s “qualifying single source drug” definition is overly broad and not supported by the statute. (Section 30.1)

CMS is defining the term “qualifying single source drug” (QSSD) broadly to include all dosage forms and strengths of the drug with the same active moiety (or for biologics, active ingredient) and the same holder of the New Drug Application (NDA) (or for biologics, Biological License Application (BLA)), inclusive of products that are marketed pursuant to different NDAs or BLAs.

CMS’s QSSD definition is overly broad and not supported by the statute. Section 1192(e)(1) of the Social Security Act (the “Act”) outlines the definitional criteria for QSSDs. For both small-molecule drugs and large-molecule biological products, the statute unambiguously anchors the QSSD definition to the *singular* approval by the Food and Drug Administration (FDA) under which the product is marketed.¹ The statute in no way authorizes CMS to convert this focus on the *singular* FDA approval to a definition that sweeps in products with multiple separate FDA approvals through the addition of an “active moiety/ingredient” test. As such, the term QSSD should be defined no more broadly than the NDA/BLA, which is the approval under which the product is originally marketed.

CMS’s reliance on section 1192(d)(3)(B) of the Act to support its aggregation of NDA/BLAs into a single QSSD is misplaced because it ignores sequential placement of the QSSD definition relative to the “total expenditures” calculation. Section 1192(d)(3)(B) of the Act describes the aggregation of *dosage forms and strengths* for purposes of calculating Parts B and D total expenditures to determine whether a drug that is *already* a QSSD qualifies as a “negotiation-eligible” drug. Section 1192(d)(3)(B) does not govern the identification of the underlying QSSD. Stated differently, section 1192(d)(3)(B) applies *after* the QSSD is identified and ensures that the different dosage forms and strengths of a QSSD are incorporated into the total expenditure calculation. This requirement is intended to account for the common circumstance where a single NDA/BLA, and even a single supplemental NDA/BLA, can have multiple dosage forms and strengths.

Additionally, CMS’s aggregate approach to defining QSSD may stymie innovation and limit patient access to new therapies that could improve their health outcomes. Pursuing FDA approval or licensure for a new product affords patient access to new scientific advances, including products that are easier to administer, have fewer side effects, or treat new indications. However, obtaining such approval involves a significant expenditure of resources, even if the new product shares the same active ingredient/moiety with an existing therapy. If CMS aggregates separate NDAs/BLAs into a single QSSD, manufacturers will be deterred from making these investments

¹ For drugs to be a QSSD, section 1192(e)(1) of the Act requires only that the drug be ““approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act and is marketed pursuant to such approval.”” Likewise for biological products, section 1192(e)(2) requires only that the biological product be ““licensed under section 351(a) of the Public Health Service Act and is marketed under section 351 of such Act.”” Canons of statutory construction suggest that a legislative drafter writes precisely and in accordance with the rules of grammar. *See, e.g.,* *Arcadia v. Ohio Power Co.*, 498 U.S. 73, 79 (1990) (“In casual conversation, perhaps, such absent-minded duplication and omission are possible, but Congress is not presumed to draft its laws that way.”) Thus, Congress’ reference to only a singular approval should be given weight. *See, e.g.,* *Niz-Chavez v. Garland*, 141 S. Ct. 1474, 1480 (2021) (emphasizing the use of “the singular article ‘a’” to conclude that the statute referred to a singular term).

that would otherwise advance the scientific understanding of disease states and bring scientific applications to bear for patients.

B. Alexion supports CMS’s policy that a generic/biosimilar for “any of the strengths or dosage forms of the potential qualifying single source drug” would disqualify the drug/biological product from the QSSD definition. (Section 30.1)

CMS states that “[i]f any strength or dosage form of a potential qualifying single source drug is the listed drug or reference product, as applicable, for one or more generic or biosimilar biological products that CMS determines are approved and marketed . . . the potential qualifying single source drug will not be considered a qualifying single source drug for initial price applicability year 2026.”²

While Alexion opposes CMS’s QSSD definition, to the extent CMS proceeds with such an overly expansive interpretation, Alexion would support CMS’s policy position in relation to the impact of generic/biosimilar competition on a QSSD. Specifically, since CMS’s QSSD definition is so broad, it is necessary (as a limiting principle) that a generic/biosimilar for *any* of the branded product’s strengths and/or dosage forms is a sufficient condition to disqualify the potential QSSD, particularly because generic/biosimilar manufacturers may not seek approval for all of the strengths or dosage forms of the branded product.

However, we do have some concerns regarding CMS’s policy with respect to confirming the presence of “bona fide” marketing of the generic or biosimilar product, which we believe exceeds the statute and will be difficult to apply in a non-arbitrary manner. In adopting this policy, CMS relies on sections 1192(e)(1)(A)(iii) and 1192(e)(1)(B)(iii) of the Act for drug products and biological products, respectively.³ While these provisions require that a generic or biosimilar be “marketed” in order for the branded product to lose its QSSD status, the term “marketed” is best understood consistent with its ordinary meaning, which is to “expose for sale in a market”⁴ or “to offer products for sale to buyers.”⁵ Nothing about the “ordinary meaning” of the term “marketed” suggests that sellers must sell the product in a “robust and meaningful” manner. CMS should not operate beyond the statute by establishing a separate “robust and meaningful competition” standard. The availability of the generic/biosimilar for purchase should be sufficient to make a determination that the product is “marketed” as required by the statute. At the very least, a single sale of the generic/biosimilar product should suffice.

C. CMS should support orphan drug development and access. (Section 30.1.1)

CMS intends to interpret the orphan drug exclusion under section 1192(e)(3)(A) of the Act as applying to a drug or biological product that must (1) be designated as a drug for only one rare

² Guidance at 10.

³ *Id.* 67-68.

⁴ Definition of “Marketed”, Merriam-Webster Online Dictionary (last accessed March 25, 2023), <https://www.merriam-webster.com/dictionary/marketed>.

⁵ Definition of “Marketed”, Cambridge Dictionary Online (last accessed March 25, 2023), <https://dictionary.cambridge.org/us/dictionary/english/market?q=marketed>.

disease or condition under section 526 of the FD&C Act and (2) be approved by the FDA only for one or more indications within such designated rare disease or condition.⁶ As described in the Guidance, all dosage forms and strengths and different formulations of the QSSD must meet the criteria for the exclusion.⁷ CMS would then use the FDA's Orphan Drug Product designation database and approvals on the FDA website to identify a qualifying orphan drug. Importantly, CMS states that it is “considering whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development.”⁸

As described below, developing drugs for rare diseases is an exceedingly challenging proposition, and many rare diseases still lack an approved therapy. It is therefore essential that CMS implement the IRA's orphan drug exclusion in a manner that encourages the continued development of rare disease drugs, consistent with the intent of the Orphan Drug Act (ODA).

While each rare disease affects a relatively limited patient population, in the aggregate, rare diseases affect a significant number of Americans. There are approximately 30 million people living with over 7,000 rare diseases in the United States, including millions of Medicare beneficiaries.⁹ Many of these rare diseases are debilitating and costly, particularly for those in minority and underserved communities, negatively affecting the quality of life not only for the patients but their families and caregivers.¹⁰ Inequities caused by delays in diagnosis and treatment access to rare disease therapies are compounded by health disparities for rare disease patients, especially those that belong to racial or ethnic minority groups.

Although there has been a significant increase in the number of drugs approved to treat rare diseases since the Orphan Drug Act (ODA) was enacted 40 years ago, over 90 percent of known rare diseases still do not have a treatment. This is due, in part, to circumstances unique to rare diseases that further complicate the extremely costly¹¹ and high-risk¹² drug-development process.

For example, it can be challenging to enroll a sufficient number of patients in clinical trials for rare diseases given small patient numbers, uneven distribution of disease across populations, and heterogeneity of diseases. It is similarly challenging to design clinical trials for rare disease populations given difficulties designating an appropriate comparator, validating novel endpoints, and obtaining sufficient data from small patient populations. Obtaining the high-quality data

⁶ *Id.* at 11.

⁷ *Id.*

⁸ *Id.*

⁹ G. Yang et al. The national economic burden of rare disease in the United States in 2019, *Orphanet J. Rare Dis.* 17:163 (2022), pp. 1-11.

¹⁰ *Id.* (finding that over half of the \$966 billion economic burden of rare disease were indirect and nonmedical costs for patients and families).

¹¹ The cost of the drug development process has been estimated to take 10 to 15 years and \$1-2 billion. I.V. Hinkson, B. Madej, E.A. Stahlberg. Accelerating therapeutics for opportunities in medicine: a paradigm shift in drug discovery *Front Pharmacol*, 11 (2020), p. 770. (defining the cost of the drug development process to include all costs borne by a manufacturer leading up to FDA-approval or a particular drug).

¹² Ninety percent of clinical trials for candidate drugs ultimately prove unfeasible. H. Dowden, J. Munro. Trends in clinical success rates and therapeutic focus *Nat Rev Drug Discov*, 18 (2019), pp. 495-496.

necessary to evaluate the clinical trial outcomes for rare diseases is also a challenge given diversity in clinical presentation, disease progress, and other patient characteristics.

Meanwhile, because many rare disease drugs are the first and/or only products for a given disease, rare diseases lend themselves to being a starting point in the translation of new scientific discoveries to clinical medicine. As data emerge, drug manufacturers sometimes identify promising new uses for existing orphan therapies – in many cases for additional orphan indications. In addition to identifying patient needs and scientific pathways, there needs to be a business case for making this investment since the exploration of new indications requires significant resources.

Alexion continues to believe that CMS can take additional actions to “best support orphan drug development” as it relates to the implementation of the orphan drug exclusion. We appreciate CMS’s focus on the importance of orphan drugs to patients who need them and support CMS implementing policies that recognize the individual contributions of each orphan indication as it evaluates Medicare spending and other negotiation factors for orphan products. We offer three approaches to help CMS best support orphan drug development and access.

- i. CMS should exclude drugs that treat indications with a collective total of fewer than 200,000 patients from the Negotiation Program to preserve the incentives for orphan drug development created by Congress in the Orphan Drug Act.*

The express purpose of the ODA, enacted by Congress in 1983, is to encourage the development of innovative pharmaceutical products to treat diseases and conditions with very small patient populations, defined by Congress as those affecting fewer than 200,000 persons in the United States.¹³ The FDA, the agency with direct oversight of this program, recognizes this clear purpose, noting that it is challenging to create treatments and cures for rare diseases, including “...the complex biology and the lack of understanding of the natural history of many rare diseases. The inherently small population of patients with a rare disease can also make conducting clinical trials difficult.”¹⁴

In passing the IRA, Congress included orphan drugs as one of just three exclusions from the QSSD definition, evincing a clear intent to preserve Congress’ longstanding support and incentives for drugs treating small patient populations, namely populations of fewer than 200,000 patients.¹⁵ CMS’ approach to implementing Congress’ exemption, however, fundamentally disrupts this purpose by leaving unprotected rare disease therapies that treat fewer than 200,000 patients even across multiple indications.

When designating a drug as an orphan drug, FDA pays careful attention to the 200,000 patient prevalence limit. Further, FDA acknowledges that a drug may show promise even in

¹³ The ODA defines the term “rare disease or condition” to mean “any disease or condition which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug.” See 21 U.S.C. § 360bb(a)(2).

¹⁴ “Rare Diseases at FDA,” Available at <https://www.fda.gov/patients/rare-diseases-fda> (Accessed April 7, 2023).

¹⁵ Section 1192(e)(1) of the Act.

multiple, different rare diseases. Such drugs may be eligible for multiple orphan designations because FDA considers the prevalence within each disease or condition. By way of example, in 2007 the FDA approved Alexion's SOLIRIS® (eculizumab) as the first therapy approved for paroxysmal nocturnal hemoglobinuria (PNH), a rare, disabling and life-threatening blood disorder defined by chronic red blood cell destruction, or hemolysis.¹⁶ Alexion has since continued to invest in advanced clinical research to bring the clinical benefits of SOLIRIS to other rare patient populations: atypical hemolytic uremic syndrome (aHUS) (in 2011),¹⁷ generalized myasthenia gravis (gMG) (in 2017),¹⁸ and neuromyelitis optica spectrum disorder (NMOSD) (in 2019).¹⁹ Using the highest U.S. prevalence numbers available, the current total estimated disease prevalence across all four conditions is estimated to be only 167,112 patients, still far fewer than the 200,000 patient size contemplated by Congress in enacting the ODA.²⁰ Yet, under CMS' interpretation of the IRA's orphan drug exclusion, the 2011 approval of SOLIRIS for aHUS in 2011 would have resulted in the loss of the orphan drug exclusion for SOLIRIS, at a time when the therapy was approved for a combined population of fewer than 500 patients nationwide across both approved indications. This would have made it difficult for Alexion to justify the significant investment necessary to obtain FDA approval for the two remaining indications had the IRA been in effect at the time.

As is clear, CMS's approach will have the effect of including in the Negotiation Program orphan drugs treating patient populations well below the 200,000 threshold Congress sought to protect in the ODA, undermining the ODA's purpose and disturbing a carefully crafted framework that has been remarkably successful in bringing new lifesaving treatments to patient populations that may otherwise have lacked access to any therapy for their rare condition.

Considering these significant concerns, we strongly urge CMS to exclude from negotiation any drug that, in aggregate, treats indications for which there are fewer than 200,000 patients in the United States.

- ii. *The orphan drug exclusion should be applied to exclude a drug from a QSSD if the drug falls within the scope of the orphan drug exclusion.*

Promulgating an orphan exclusion that focuses on broad targeting of orphan drugs for negotiation will mean fewer products qualify for the orphan drug exclusion and harms patients by discouraging the continued development of orphan drugs. We oppose the agency's interpretation

¹⁶ See FDA Approval Letter for Soliris (available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2007/125166s0000_LTR.pdf.)

¹⁷ FDA Approval Package for Soliris for the treatment of aHUS (available at https://www.accessdata.fda.gov/drugsatfda_docs/bla/2011/125166Orig1s172-2.pdf).

¹⁸ FDA Approval Package for Soliris for the treatment of gMG (available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/125166Orig1s422.pdf).

¹⁹ FDA Approval Package for Soliris for the treatment of NMOSD (https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/125166Orig1s431.pdf).

²⁰ Analysis conducted based on disease prevalence numbers reported in the National Organization for Rare Disorders' Rare Disease Database (available at <https://rarediseases.org/rare-diseases>).

of the orphan drug exclusion on these grounds, and because it is inconsistent with the statutory requirements of the IRA.

Under CMS's policy, an orphan drug approved under a separate NDA/BLA would not fall within the scope of the orphan drug exclusion if it were aggregated into a broad QSSD with non-orphan products with the same active ingredient/moiety, which would discourage the development of orphan drugs. Specifically, because CMS has adopted an overbroad interpretation of QSSD, which is defined by reference to the active ingredient/moiety, a single QSSD could include multiple drugs approved under separate NDAs/BLAs. As a practical matter, it is possible that only one such drug qualifies for the orphan drug exclusion (i.e., approved by FDA only for one or more indications within a single rare disease or condition).²¹ However, CMS would prevent that drug from benefitting from the orphan drug exclusion by requiring that “all dosage forms and strengths and different formulations” of the QSSD into which the orphan drug is aggregated meet the orphan drug exclusion. Such a result effectively discourages developers from developing new therapies and runs contrary to Congress’ decision to exclude orphan drugs from negotiation.

Such a read is also inconsistent with the statutory text of the orphan drug exclusion. Section 1192(e)(3)(A) of the Act provides that the term “qualifying single source drug” does not include “a drug” that is “designated as a drug for only one rare disease or condition under section 526 of the Federal Food, Drug, and Cosmetic Act and for which the only approved indication (or indications) is for such disease or condition falls within the orphan drug exclusion.” This language excludes a drug from inclusion in a QSSD if the drug falls within the orphan drug exclusion. Stated differently, the statute contemplates that CMS would first identify the full potential scope of the QSSD, and then subsequently apply the orphan drug exclusion to exclude qualifying orphan drugs from inclusion therein. Therefore, if CMS proceeds with a broad interpretation of QSSD that includes all dosage forms and strengths of the same active moiety or active ingredient—inclusive of products that are marketed pursuant to different NDAs or BLAs from the same market authorization holder—CMS should exclude from a QSSD any products marketed under a distinct NDA or BLA which are individually eligible for the orphan drug exclusion.

This approach may help preserve incentives to continue to develop orphan drugs and avoids arbitrarily failing to apply the orphan drug exclusion to qualifying drugs based solely on their aggregation into a QSSD with other non-qualifying drugs.

- iii. *The 7- or 11-year period that must elapse before a drug or biological can be subject to negotiation should begin on the date a drug loses eligibility for the orphan drug exclusion.*

²¹ We note that CMS’s interpretation of the orphan drug exclusion could be read as precluding a drug with multiple orphan drug designations (ODDs) from qualifying for the exclusion, even if only one of the ODDs had any approved indications. Alexion strongly opposes this read of the statute, which would further discourage the development of therapies for rare disease by creating an incentive not to seek multiple ODDs, and even to withdraw ODDs already rewarded. We therefore urge CMS to focus only on approved indications in applying the orphan drug exclusion.

In the case of a drug that initially qualifies for the orphan drug exclusion from inclusion in a QSSD, as described above, CMS should clarify that the 7- or 11-year period prior to negotiation eligibility begins to run only upon the loss of the orphan drug exclusion.

As discussed above, pursuant to section 1192(e) of the Act, a drug can only be classified as a QSSD (and hence be subject to negotiation) once “*at least 7 years...since the date of such approval [under section 505(c)]*” or “*at least 11 years...since the date of such licensure [under section 351(a)]*” have elapsed. This language must be read in the context of the orphan drug exclusion, which provides that: “[T]he term ‘qualifying single source drug’ does not include any of the following . . . [a] drug that is designated as a drug for only one rare disease or condition under section 526 of the [FDCA] and for which the only approved indication (or indications) is for such disease or condition.”²²

Under CMS’s guidance, a drug that initially qualifies for the orphan drug exclusion would lose this exclusion, and could potentially be classified as a QSSD, following the approval, with respect to the same active moiety, of a non-orphan indication or a new orphan indication for a distinct disease or condition. CMS’s guidance, however, does not address *when* such a drug could potentially be classified as a QSSD and hence become eligible for negotiation.

CMS should issue additional guidance to clarify that the orphan drug exclusion entirely insulates a product from the IRA’s negotiation provisions for the entire duration the exclusion applies. Thus, the 7- or 11-year pre-negotiation period would commence only upon the date a drug loses eligibility for the orphan drug exclusion. This outcome is supported by the statute’s plain language and scheme.

Notably, the orphan drug exclusion constitutes a threshold exclusion from the definition of a QSSD.²³ It must follow from this structural placement that the 7- or 11-year pre-negotiation period that would otherwise apply to a QSSD is *tolled* until the first day after the orphan drug no longer meets the requirements of the orphan drug exclusion. Indeed, any other approach would defeat the intent of excluding relevant orphan drugs from the QSSD definition, including the statutory sub-elements. (Consider, by contrast, the small-biotech exclusion, which was specifically inserted as an exclusion to the definition of a “*negotiation-eligible drug*” under section 1192(d)(2) of the Act.)²⁴

By issuing guidance that sets forth the interaction between the orphan drug exclusion and the QSSD definition in this way, CMS will be following the plain text of the statute. Additionally, we believe that CMS should interpret the Medicare Negotiation program in a way

²² See SSA § 1192(e)(3)(A).

²³ See SSA § 1192(e)(3)(A) (“Exclusions.—In this part, the term [QSSD] does not include any of the following... (A) Certain Orphan Drugs.”)

²⁴ See SSA § 1192(d)(2) (stating that “term ‘negotiation-eligible drug’ shall not include... a qualifying single source drug that meets [the listed criteria]”).

that supports and safeguards the important progress the ODA has achieved in sharing the benefits of medical innovation with patients with orphan diseases. The approach outlined here better enables innovator companies to pursue orphan indications by initiating the pre-negotiation period only upon a subsequent approval for a distinct disease or condition.

II. Section 50: Negotiation Factors

Alexion supports CMS's solicitation of information from patients and Medicare beneficiaries to inform the negotiation process and urges CMS to give substantial weight to the patient voice. We further support CMS's policy of not considering quality-adjusted life years (QALYs) for purposes of the Negotiation Program and the agency's close scrutiny of any comparative effectiveness research that may rely on QALYs for its conclusions. However, we urge CMS to allow for manufacturer input regarding the selection of therapeutic alternatives, and to develop a more detailed framework for how the agency will consider therapeutic alternative and comparative effectiveness data based on five core principles, discussed below.

A. Alexion supports CMS's solicitation of information from patients and Medicare beneficiaries and urges CMS to give substantial weight to the patient voice (Section 50.2).

As described in the Guidance, CMS will consider therapeutic alternative and comparative effectiveness data submitted by Medicare beneficiaries, academic experts, clinicians, and other interested members of the public.²⁵ We strongly support this solicitation, and we note that the patient voice is often ignored, even in the comparative effectiveness research that purports to assess the best treatments for patients. This is particularly true for people of color with rare diseases, who face additional disparities in access to care, including differences in health care utilization, delayed or missed care due to a lack of transportation or work flexibility, and a lack of representation in clinical trials and research. Alexion therefore urges CMS to give substantial weight to the patient experience in CMS's evaluation of therapeutic alternatives and comparative effectiveness. Factors such as patient convenience due to route of administration, caregiver burden, and improvements in quality of life not otherwise measured by endpoints in a clinical trial nevertheless represent a significant benefit to the patient experience. Such a seemingly innocuous benefit can directly impact other health outcome metrics, such as medication adherence and patient self-sufficiency through an improved ability to consistently engage in gainful employment. We urge CMS to not only take into account the beneficiary and caregiver experience, but to prioritize it when evaluating the value of a drug product.

B. Alexion supports CMS's policy of not considering QALYs in applying comparative effectiveness research. (Section 50.2)

As required by statute, CMS will assess a selected drug's comparative effectiveness as compared to "therapeutic alternatives."²⁶ In so doing, CMS stated the agency will not use evidence from comparative clinical effectiveness research that treats extending the life of an individual who

²⁵ *Id.*

²⁶ *Id.* at 36.

is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill, including quality-adjusted life years (QALYs).²⁷ To the extent that studies regarding comparative effectiveness employ QALYs in its analysis, CMS will not consider it unless it is able to separate such evidence.²⁸ Alexion supports CMS's policy of not considering QALYs for purposes of the Negotiation Process, which is consistent with the plain statutory language of the IRA. We similarly support the agency's close scrutiny of any comparative effectiveness research that may rely on QALYs for its conclusions.

C. CMS should allow for manufacturer input on the selection of therapeutic alternatives. (Section 50.2)

Alexion further urges CMS to allow for manufacturer input into the selection of therapeutic alternatives in applying comparative effectiveness research as part of the Negotiation Program. In the Guidance, CMS outlines a flexible approach to considering therapeutic alternatives and evaluating comparative effectiveness. We note that Alexion has serious concerns that certain studies have drawn improper comparisons across therapies. As a result, we have a number of open questions including, for example: Will CMS consider products that treat the same disease area, or that treat the same specific indication, as therapeutic alternatives? How will CMS distinguish between different mechanisms of action or routes of administration, even when the drugs under consideration treat the same disease area or specific indication? How will CMS consider comparative effectiveness research in light of demonstrable differences in heterogeneous patient populations where what may work for one patient may not work for another, thereby confounding the comparability of comparative effectiveness comparisons? How does CMS intend to resolve conflicting evidence as it relates to a selected drug's comparative effectiveness?

Given these significant uncertainties, at a minimum Alexion urges CMS to provide manufacturers with an opportunity to engage with CMS and review CMS's methodology for the selection of therapeutic alternatives before CMS makes such a determination. We also urge CMS to consider only on-label indications in selecting therapeutic alternatives, as off-label indications have not been approved by FDA and have significantly less robust data regarding safety and efficacy, relative to on-label uses.

D. CMS should develop a more detailed framework for how the agency will consider therapeutic alternative and comparative effectiveness data based on five core principles (Section 50.2)

As described in the Guidance, CMS will consider therapeutic alternative and comparative effectiveness data submitted by Medicare beneficiaries, academic experts, clinicians, and other interested members of the public. Assessment of a treatment's clinical value should be a shared endeavor between CMS and pharmaceutical manufacturers. Alexion supports a framework for assessment of clinical value that considers the following five core principles:

²⁷ *Id.*

²⁸ *Id.*

1. **The process of clinical value assessment should be transparent.** Using scientific principles, a consistent methodology, and appropriate evidence, various stakeholders should be able to come to similar conclusions.
2. **While adhering to a consistent methodology, clinical value assessments should consider contextual factors associated with the disease in question.** This is particularly important for rare diseases. Aside from the obvious recruitment challenges in rare disease clinical trials, the basic pathophysiology of many rare diseases is less well understood compared to more common diseases. Because of this, clinical trials for rare disease treatments often use endpoints that are not specifically developed to capture the full impact of the rare disease or its treatment. In generalized Myasthenia Gravis, for instance, the primary endpoint focuses on physical aspects of the disease, just one of eight domains patients reported that are impacted by the disease.
3. **Appropriate therapeutic alternatives must be assessed, based on clinical, not economic factors.** Therapeutic alternatives should be licensed and approved for the disease in question and there should be sufficient data to make a valid assessment of each alternative's clinical value feasible. For many rare diseases with existing treatments, there may be only one appropriate therapeutic choice. And, as noted above, the manufacturer should have input regarding the identification of therapeutic alternatives.
4. **The perspective of clinical value assessment should be holistic.** The assessment must include not just short-term efficacy endpoints used in clinical trials, but safety, long-term health outcomes, patient experience factors such as route and frequency of administration, impacts on population health equity, health system resource use, and societal impacts outside the healthcare system as well. A study conducted by the EveryLife foundation²⁹ concluded that 55 percent of the total burden of rare diseases is experienced outside of the healthcare system. But these impacts outside the healthcare system are still very much part of the lived experience of rare disease patients. In NMOSD, the primary endpoint in clinical trials is the reduction in relapses. What remains unmeasured, however, is how the reduction of debilitating attacks on nerves in the eye and the spine allows patients to continue to earn a living or live a life without fear of the next attack. Equity deserves additional consideration. Evidence in generalized Myasthenia Gravis shows non-white patients are diagnosed and treated with a delay of many years, often initiating treatment with a higher level of disease activity. Access to treatment options for these patients may address a disproportionately higher unmet medical need.
5. **The data to inform a holistic perspective of clinical value will necessarily need to come from a wide range of sources.** Appropriate data sources should include, but should not be limited to, clinical trials, patient registries, and other real-world data. Here again, consideration of disease rarity will be important because real-world data is more challenging to collect for rare disease. Despite this, patient registries and other real-world

²⁹ Yang et al. Orphanet Journal of Rare Diseases (2022) 17:163.

data have been important sources of data to demonstrate the value of rare diseases treatments. For example, after asfotase alfa was associated with a significant improvement in survival among infants with hypophosphatasia (HPP) and bone health among children with HPP within our clinical trials, the Global HPP Registry has subsequently demonstrated that adults with HPP treated with Strensiq® (asfotase alfa) in real-world settings experience significant improvements in physical function and quality of life. Real-world data are also needed to assess some endpoints not easily measured in clinical trial settings, such as caregiver burden and non-medical costs.

III. Section 60: Negotiation Process

A. CMS should holistically consider a selected drug’s clinical value, rather than narrowly focusing on R&D spend and recoupment. (Section 60.3).

As described in section 60 of the Guidance, CMS is proposing a four-step process to determine an initial offer and counteroffer for a selected drug. Specifically, CMS intends to: (1) identify indications for the selected drug and therapeutic alternative(s); (2) use as a starting point the Part D net price for Part D drug therapeutic alternative(s) and/or Part B average sales price for Part B therapeutic alternative(s); (3) evaluate clinical benefits of the selected drug to adjust the starting point; and (4) further adjust the preliminary price through consideration of manufacturer-specific data (e.g., R&D costs; current unit costs of production and distribution) to determine the initial offer price. While Alexion supports CMS’s proposal to prioritize the consideration of clinical benefits, we are concerned that the proposed methodology does not predictably recognize therapeutic advances or treatment options that address unmet needs.

First, we are concerned that CMS may be putting undue weight on certain manufacturer-specific factors. For instance, CMS is seeking extensive information on manufacturer R&D costs as well as global recoupment of development costs. This raises the concern that the extent to which manufacturers have recouped development costs will have undue weight on the price of selected drugs. Although obviously very important to drug discovery and development, the amount of R&D costs for a drug are not necessarily indicative of the drug’s value. Indeed, while developers may expend large R&D investments to develop a product that ultimately brings tremendous clinical value, products with lower R&D spend can have an equal or greater value. Conversely, products with significant R&D costs may not work any better than the current standard of care, or only marginally better.

Alexion acknowledges that CMS is required by statute to take into consideration certain factors—including R&D costs—in setting the maximum fair price (MFP) for a selected drug. However, such factors are to be considered only “as applicable to the drug” and not all the statutory negotiation factors must be weighted equally. More importantly, we are concerned that CMS’s proposed approach will undervalue innovative selected drugs, including therapies approved to treat rare diseases. If the MFP for meaningful clinical improvements is set too low, investment in both initial and post-approval R&D will decline, resulting in reduced access to needed therapies for patients.

As also noted in our comments regarding section 60.3.3 and 60.3.4 of the Guidance, below, Alexion urges CMS to instead prioritize the negotiation factors described in section 1194(e)(2) of the Act. Specifically, CMS should establish the MFP at the ceiling price for products that, over the course of the product's lifecycle, have provided therapeutic advancements or treated previously unmet medical needs. This approach would best preserve incentives for the development of orphan drugs, establish a clear and predictable methodology for determining drug pricing, and enable CMS to meet its statutory obligations under the IRA.

B. CMS should allow for manufacturer input on the selection of therapeutic alternatives for purposes of identifying the “starting point” for the initial MFP offer calculation. (Section 60.3.1).

As described above, CMS is proposing a four-step process to determine an initial offer and counteroffer for a selected drug. To the extent CMS retains this framework, we have some concerns regarding how it might be implemented. For instance, as to this first step, as described in response to our comments to section 50.2, above, manufacturers should be given an opportunity to weigh in regarding CMS's selection of therapeutic alternatives as certain studies have drawn improper comparisons across therapies. In addition, an off-label product is priced for use in its licensed indication, making its price an unsuitable starting point for negotiations.

C. CMS should start with the ceiling price rather than the Federal Supply Schedule (FSS) or “Big Four Agency” pricing when there are no therapeutic alternatives or pricing for the therapeutic alternatives is above the ceiling price. (Section 60.3.2)

As to the second step, CMS intends to use the Part D net price(s) and/or average sales price(s) (ASP(s)) of therapeutic alternative(s) for the selected drug as the starting point for developing the MFP initial offer unless the resulting price is higher than the statutory ceiling.³⁰ Where there is no therapeutic alternatives available on the market, or where the pricing for the therapeutic alternatives is greater than the statutory ceiling price, CMS intends to determine the starting point for the initial offer based on the FSS or “Big Four Agency” pricing.³¹

Alexion opposes CMS's proposed use of the FSS or “Big Four Agency” pricing as the “default” starting point for the initial offer for those products with no therapeutic alternative. Many therapies for rare disease fall into this category, and the FSS and “Big Four Agency” prices do not reflect market pricing, as these pricing benchmarks incorporate significant and mandatory price cuts that would otherwise undermine patient access in a market setting. The use of the FSS or “Big Four Agency” prices as the default starting point thus arbitrarily punishes manufacturers that develop drugs for patients who lack therapeutic alternatives. If anything, the starting point for these products should be *higher* than products that have therapeutic alternatives. CMS should therefore use the statutory ceiling price as the starting point in such circumstances, consistent with the underlying statutory language. Unlike FSS and “Big Four Agency” pricing, the statutory

³⁰ *Id.* at 48.

³¹ *Id.* at 49.

ceiling price is a market-based price that more closely approximates the starting price point for other therapies.

D. CMS should provide a clearer framework for how the clinical factors will be used to establish the MFP. (Section 60.3.3)

After identification of therapeutic alternatives for purposes of establishing a starting point for negotiation, CMS intends to adjust the starting point based on the clinical benefit that the selected drug confers as compared to its therapeutic alternatives. CMS will broadly evaluate the body of clinical evidence through a CMS-led literature review, and CMS may also analyze Medicare claims data or other pharmaceutical drug datasets for utilization patterns, clinical data, or other information relevant to the selected drug and its therapeutic alternatives. CMS's adjustments to the starting point will be referred to as the “preliminary price.”

As noted above, we recommend that CMS set the MFP at the ceiling price for selected drugs that, over the course of the product's life cycle, have provided therapeutic advancements or treated previously unmet medical needs. For other products, we believe CMS should provide clearer guidance on the specific elements that will be evaluated, the weight applied to any one individual element, and the directional adjustments that CMS would make based on its evaluation of such elements and their relative weight.

Any determination of clinical benefit or of unmet medical need must also explicitly include a framework for weighing the patient and caregiver voice and lived experiences, in addition to clinical factors such as disease prognosis and the lack of alternative therapies. While patient and caregiver voices are important in the consideration of any therapy's advantages, these voices are doubly important in the context of diseases without therapeutic alternatives. This is often the case for rare disease, as 90 percent of rare diseases currently lack an approved therapy.

E. CMS should apply special considerations when evaluating selected drugs, such as orphan drugs due to their unique circumstances. (Sections 60.3.3)

We appreciate that CMS has, elsewhere in the Guidance, recognized the need to work with stakeholders to “support orphan drug development.”³² As a leader in rare disease treatment development, we are deeply interested in ensuring that CMS's clinical benefit assessment for selected drugs without therapeutic alternatives is appropriately calibrated to account for the unique characteristics of rare disease and to appropriately recognize the value of orphan drugs. As CMS develops a clinical benefit assessment for selected drugs that are orphan drugs, it must do so with a recognition that rare diseases are rare and diverse, and thus tend to be less well understood than therapies for more common disease. CMS should similarly adopt special considerations that recognize some of the data and other limitations associated with orphan therapies.

F. Manufacturer-specific factors should not be used for drugs that represent a therapeutic advance or address an unmet need (Section 60.3.4).

³² *Id.* at 11.

As to the fourth step in the process, as described our comments in response to Section 60.3.3, above, Alexion urges CMS to prioritize the clinical negotiation factors. Specifically, CMS should focus on whether a selected drug demonstrates a clinical benefit and addresses an unmet need in calculating the MFP. To avoid setting the MFP too low, CMS should not incorporate the manufacturer-specific factors unless a product does not address an unmet need or represent a therapeutic advance over its therapeutic alternatives. As noted above, this approach would best preserve incentives for innovation, establish a clear and predictable methodology for determining drug pricing, and enable CMS to meet the statutory obligations of the IRA.

* * * * *

We thank CMS for considering our comments. Please contact Lisa Feng at lisa.feng@alexion.com if you have any additional questions about our comments.

Sincerely,



Lisa Feng, Senior Director, Health Policy
Alexion, AstraZeneca Rare Disease

April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Blvd
Baltimore, MD 21244

**Re: Medicare Drug Price Negotiation Program: Initial Memorandum,
Implementation of Sections 1191 – 1198 of the Social Security Act for Initial
Price Applicability Year 2026, and Solicitation of Comments**

Dear Dr. Seshamani,

The Alliance for Aging Research (“Alliance”) appreciates the opportunity to review and comment on the initial guidance regarding the implementation of the Medicare Drug Price Negotiation Program. The Alliance is the leading nonprofit organization dedicated to accelerating the pace of scientific discoveries and their application to vastly improve the universal human experience of aging and health.

The Alliance actively supported several provisions in the Inflation Reduction Act of 2022—expansion of the low-income subsidy program; reducing beneficiary costs for vaccination; an inflationary cap; and most notably, the Medicare Part D provisions restructuring the benefit and adding a much-needed annual cap on out-of-pocket costs. However, since 2019, the Alliance has consistently urged federal policymakers to reject reliance on cost-effectiveness methodologies that discriminate against older adults and persons with a disability – the very populations that Medicare serves. As CMS implements the price negotiation provisions of the IRA, it is vital that the agency avoid

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the use of such methodologies and instead focus on use of patient-centered value assessment techniques.

Our concerns regarding implementation without due consideration of potential beneficiary impacts—including significantly decreased access to necessary drugs, therapeutics, and other forms of care—remain, and we have outlined them in our comments below. We thank CMS for the opportunity to provide feedback and suggestions to ensure that any potential negative impacts of the Medicare Drug Price Negotiation Program (“Negotiation Program”) on patient access to care are avoided or mitigated.

§50.2 and §60.3.3: Indirect Use of the Quality-Adjusted Life Year and Other Similar Metrics

The older adult and disability communities have communicated at length about the discriminatory impacts of the quality-adjusted life year (QALY) on patient access to care. While the Alliance supported the QALY-related language in the Inflation Reduction Act of 2022, it did not go far enough. The language states, “the Secretary shall not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, non- disabled, or not terminally ill”. Further, this language did not communicate the full extent to which the law forbids CMS from using QALYs in the negotiation process. Previously-established statutory language from the Affordable Care Act (ACA) states:

”The Patient-Centered Outcomes Research Institute established under section 1181(b)(1) shall not develop or employ a dollars-per-quality adjusted life year (or similar measure that discounts the value of a life because of an individual’s disability) as a threshold to establish what type of health care is cost effective or recommended. **The Secretary shall not utilize such an adjusted life year**

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(or such a similar measure) as a threshold to determine coverage, reimbursement, or incentive programs under title XVIII.”¹

The language in the initial guidance does not go far enough to meet the standard set forth in the ACA in relation to avoiding use of the QALY for coverage or reimbursement decisions in the Medicare program. Further, the National Council on Disability (NCD), an independent federal agency, has noted that use of the QALY and similar measures would undermine major disability and civil rights laws, including the Americans with Disabilities Act.² Further, there are similar metrics that operate similarly to the QALY that CMS should avoid using in the Negotiation Program to ensure that the metrics used to assess value support the provision of equitable, fair, and nondiscriminatory healthcare in the Medicare program.

In the draft guidance, the Medicare program has stated that reports that use QALYs will likely be a tool and reference point for price-setting, indicating that complimentary metrics like the estimated value of life years gained (evLYG) and conclusions drawn from incomplete data and discriminatory assumptions are still on the table for consideration. However, when the output of these methodologies is used, it has detrimental impacts on patient access, patient-centered care, and shared decision-making. In the initial guidance, CMS proposed the following:

“Information submitted ... that treats extending the life of individuals in these populations as of lower value, for example certain uses of quality-adjusted life-years (QALYs), will not be used in the negotiation process. In instances where a study uses QALYs in a life-extension context but has clearly separated this use of QALYs from other evidence in the report (e.g., clinical effectiveness, risks, harms,

¹ Social Security Administration. “Limitations on Certain Uses of Comparative Clinical Effectiveness Research.” https://www.ssa.gov/OP_Home/ssact/title11/1182.htm

² National Council on Disability. “Quality-Adjusted Life Years and the Devaluation of Life with Disability: Part of the Bioethics and Disability Series.” 6 Nov 2019. https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

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etc.) that is relevant to the factors listed in section 1194(e)(2) of the Act, CMS intends to consider such separate evidence. CMS will ask entities submitting information to indicate whether or not their submission contains information from studies that use QALYs in a life-extension context.

We have deep concerns that CMS has expressed interest in utilizing QALYs as long as they are not used in a “life extension context.” Though the IRA language speaks to life extension only, this does not abrogate the clear prohibition on the use of QALY and similar metrics in Medicare’s coverage and reimbursement decisions codified in the ACA. It is troubling that the draft guidance proposes an intent to include direct or indirect application of discriminatory cost-effectiveness standards, including contracting with these third-party organizations such as the Institute for Clinical and Economic Review (ICER) that have adopted and endorsed the use of these metrics.

Clearly stated, CMS should not utilize information that includes reference to the QALY, even if its use is not specific to life extension.

In light of the ban on QALYs, ICER and the organization’s allies³ are advocating that Medicare use the equal value life years gained metric (evLYG) in the Negotiation Process, characterizing the evLYG as an alternative to the QALY. However, these perspectives fail to acknowledge the major pitfalls of the evLYG. The evLYG was never intended to be used as a standalone metric, it was developed to serve in partnership with the QALY and to be compared when the outcomes of the evLYG analysis differed starkly from the QALY. Because of this, the evLYG maintains the same discriminatory lineage as the QALY. The only difference between the evLYG and the QALY is that the evLYG uses a static health state preference value of .85 as opposed to using values that vary by condition. The calculation is done in the same way for both—by multiplying the amount

³ Frank, Richard G; and Nichols, Len M. “Threats to Medicare’s new drug negotiation power.” USC-Brookings Shaeffer Initiative for Health Policy Blog. 15 Mar 2023. <https://www.brookings.edu/blog/usc-brookings-schaeffer-on-health-policy/2023/03/15/threats-to-medicare-new-drug-negotiation-power/>

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of time patients are likely to spend in their disease state.⁴ As a result, the evLYG maintains its discriminatory effects. The underlying assumption in both metrics is that older adults have fewer life years to gain than younger individuals from the use of therapeutics. As a result, any condition that disproportionately impacts the aging population will be evaluated as being of lower value than therapeutics whose evLYG is calculated based on a relatively younger population.

Further, the evLYG does not accurately take into account the heterogeneity of patient groups, leaving “quality of life” out of the equation entirely. This choice is marketed as the solution to the improper calculation of quality found in the QALY framework, but leaving this process out entirely does not solve the issue. By not considering the value of quality of life at all, the evLYG measure has no sensitivity given to the alleviation of side effects, symptomatic treatment, or a treatment’s method of distribution. All of these factors play a role in a therapeutic’s value to patients.

Neither the NCD nor the Disability Rights Education and Defense Fund (DREDF) endorses the evLYG, with the DREDF saying, “Neither [the evLYG or the QALY] accounts for both the full value of life-extension and the value of quality of life improvement.” The NCD notes that under the evLYG system, “denial of coverage is still possible, even where a drug would provide significant clinical benefit including life extension.”⁵ Further, methods for the underlying data collection and analysis of the evLYG are incomplete and immature. At present, groups like ICER rely solely on clinical trial data, which typically include exclusion criteria that disqualify individuals from participating in a trial based on comorbidities, age, and other factors. As a result, clinical trial data often reflects a population that differs significantly from real-world users,

⁴ O’Day, Ken and Mezzio, Dylan. “Demystifying ICER’s Equal Value Life Year’s Gained Metric.” Value & Outcomes Spotlight. Feb 2021. <https://www.ispor.org/publications/journals/value-outcomes-spotlight/vos-archives/issue/view/overcoming-vaccine-hesitancy-injecting-trust-in-the-community/demystifying-icer-s-equal-value-of-life-years-gained-metric>

⁵ National Council on Disability. “Quality-Adjusted Life Years and the Devaluation of Life with Disability: Part of the Bioethics and Disability Series.” 6 Nov 2019. https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

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meaning that any calculations of evLYG is not representative of a drug's entire intended user base.⁶ Further, the evLYG fails to assess treatments that improve quality of life as cost-effective.

Therapeutics evaluated based only on – or for which a price is benchmarked based upon – criteria consistent with traditional cost-effectiveness analysis (CEA) suffer because they can be unfairly and poorly subjected to utilization management practices, lower formulary placement or being left off a formulary all together, resulting in higher co-payments for patients or denial of coverage. Considerations that may be left out by traditional CEA include, “a new therapy's ability to treat a previously inadequately treated illness; its ability to broaden therapeutic options for diseases with great variability in treatment response; the possibility of cure and the importance of hope related to it; the ease of a regimen when alternative therapies are complex, cumbersome, and time consuming; or, its novel mechanism of action that could lead to markedly improved derivative treatments.”⁷ **We ask that the Medicare program meaningfully consider the heterogeneity of treatment effects, sensitivity assessments, and not rely on reports that tout evidence from traditional CEA models like the QALY or evLYG. It is unacceptable to rely on these models when there are suitable alternatives that do not reference discriminatory methodologies.**

Price Matching with the Department of Veterans Affairs

The Alliance is also concerned that CMS may utilize the prices paid by the Department of Veterans Affairs (VA) to help establish the negotiated price for drugs in Medicare. In 2017, the VA entered into a cooperative agreement with ICER as a component of the formulary development process and to assist in setting benchmarks for price

⁶ Institute for Clinical and Economic Review. “2020-2023 Value Assessment Framework.” 31 Jan 2020.

https://icer.org/wp-content/uploads/2020/11/ICER_2020_2023_VAF_02032022.pdf

⁷ Dubois, Robert W. CVS To Restrict Patient Access Using Cost-Effectiveness: Too Much, Too Soon. Health Affairs. 17 Sept 2018. <https://www.healthaffairs.org/doi/10.1377/forefront.20180913.889578/full/>

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negotiation.⁸ Therefore, referencing the VA’s negotiated prices would inappropriately incorporate and adopt the use of the QALY, which would be antithetical to the language in the ACA that prohibits QALY use for the Medicare program. Further, a 2020 report from the Government Accountability Office noted that the two programs have “very different authorities to bargain and negotiate with drug manufacturers and other market participants.”⁹ As a result of these differences, the VA formulary is significantly narrower than that of Medicare Part D. This narrower formulary is not preferred by Medicare beneficiaries – in fact, a 2021 Morning Consult survey commissioned by the Alliance indicated that only one in five older adults would be willing to trade their current prescription drug coverage for a system resembling the VA’s formulary.¹⁰

Alternative Methodologies for Consideration

There are many other methodologies and perspectives that are useful in determining a maximum fair price (MFP). Several groups are working to define value assessment in ways that do not discriminate and are working to actively identify and quantify endpoints that are meaningful to patients. The Patient Centered Outcomes Research Institute (PCORI) was established through the Affordable Care Act and focuses on comparative clinical effectiveness research. PCORI’s approach to value assessment calls for consideration of economic impacts as a part of the larger whole of outcomes that matter to patients and caregivers.¹¹ Other groups are also working to develop consensus-based principles on the most effective methods for value assessment, including specific efforts to address health equity. The Innovation and Value Initiative (IVI) has identified four areas where value assessment has failed to address equity, including lack of

⁸ Institute for Clinical and Economic Review. ICER’s Collaboration with the Department of Veterans Affairs. <https://icer.org/who-we-are/history-impact/impact-case-study-2/>

⁹ Government Accountability Office, “Prescription Drugs: Department of Veterans Affairs Paid About Half as Much as Medicare Part D for Selected Drugs in 2017.” Dec 2020. <https://www.gao.gov/assets/gao-21-111.pdf>

¹⁰ Alliance for Aging Research, New Poll Highlights Seniors’ Priorities and Concerns in Prescription Drug Pricing Legislation, Misalignment with Congress on Definition of Negotiation. 22 Sept 2021. <https://www.agingresearch.org/news/new-poll-highlights-seniors-priorities-and-concerns-in-prescription-drug-pricing-legislation-misalignment-with-congress-on-definition-of-negotiation/>

¹¹ Patient Centered Outcomes Research Institute. “About PCORI.” <https://www.pcori.org/about/about-pcori>

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incorporation in study objectives, non-representative patient participation, an absence of analysis of impacts across segments or subpopulations, and missing data on patient preferences from communities of color.¹² To address these identified issues, the IVI is now working to develop best practice protocols to inform value assessors and help mitigate these gaps.

The Medicare program *is not required* to use CEA to set a maximum fair price. There are many alternatives; this includes cost-benefit analysis, in which the dollar value of the health outcomes of a treatment are subtracted from the cost of a treatment, which the NCD notes could be a potential alternative to QALY based CEA.¹³ It is imperative that the Medicare program be discerning and ensure that discriminatory methodologies are not being used at any point during the price setting process, that decisions are only made where there is robust clinical evidence, and that patient voices are included in the process. Before an MFP is finalized, calculations must be done to ensure that patient access to care is prioritized and maintained. **Overall, if the new MFP lessens patient access based on methodologies placing a lower value on conditions affecting older adults or individuals with a disability, it is not a fair price at all.**

§60: Involving patients more substantially in the process

In its press release on its recent guidance on the Medicare Drug Price Negotiation Program for Price Applicability Year 2026, CMS publicly committed¹⁴ “to collaborating and engaging with the public” on Medicare negotiation, including involving “patients

¹² Innovation and Value Initiative. “Health Equity Initiative: How Patient Engagement and Innovation of Methods Can Move Us Closer to Achieving Health Equity.” 10 Aug 2022. Health-Equity-Initiative-Overview.pdf (thevalueinitiative.org)

¹³ National Council on Disability. “Quality-Adjusted Life Years and the Devaluation of Life with Disability: Part of the Bioethics and Disability Series.” 6 Nov 2019.

https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

¹⁴ Centers for Medicare and Medicaid Services. HHS Releases Initial Guidance for Historic Medicare Drug Price Negotiation Program for Price Applicability Year 2026. 15 Mar 2023. <https://www.cms.gov/newsroom/press-releases/hhs-releases-initial-guidance-historic-medicare-drug-price-negotiation-program-price-applicability>

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and consumers.” Additionally, throughout Section 60 of this guidance, CMS mentions several times that it will consider the “patient experience” in the Negotiation Program’s implementation.

We commend CMS for having an open-door policy to patient groups throughout this process and have appreciated the opportunity to share the Alliance’s perspective as CMS navigates implementation of the IRA. We hope that the role for the patient voice and perspective will become more formalized as this process continues in order to allow a broad representation of patient groups the opportunity to meaningfully engage. Any decisions made must keep the patient in mind. In order to do so, the patient voice must be heard, understood, and acted upon.

CMS should develop a patient engagement infrastructure that creates an ongoing dialogue about IRA implementation and systemic issues with those most affected by them. This should include:

- Creating a patient ombudsman charged with oversight of implementation;
- Convening public roundtables of disease or treatment-specific experts from the patient and disability communities for each drug selected for MFP negotiation;
- An Administrator-level Patient Advisory Committee for overall feedback on this program and other work of the Agency;
- Publicly posting all comments; and
- Seeking input from diverse communities in order to gain insights and information on the priorities and needs of those subpopulations.

Further, we ask that CMS announce a plan to ensure that the impacts of negotiation on patients will be studied following implementation and that comments will be solicited from stakeholders, including the patient community, on this topic. This study should include quantitative metrics to assess patient access to care before and after negotiation, and look to meaningfully engage the patient community in the process of developing

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solutions to any beneficiary experience problems that may occur. This study should include quantitative metrics to assess patient access to care before and after negotiation and look to meaningfully engage the patient community in the process of developing solutions to any beneficiary experience problems that may occur.

§60.3.3: Definition of unmet medical needs

In the initial guidance, meeting “unmet clinical need” is defined as “treating a disease or condition in cases where very limited or no other treatment options exist.” This definition is not nearly as expansive as the FDA’s definition for unmet clinical need. FDA defines unmet need as a “condition whose treatment or diagnosis is not addressed adequately by available therapy.” FDA notes that a new treatment generally would be considered to address an unmet medical need if it, for example, “has an improved effect on a serious outcome(s) of the condition compared with available therapy,” “has an effect on a serious outcome of the condition in patients who are unable to tolerate or failed to respond to available therapy,” or “provides safety and efficacy comparable to those of available therapy but has a documented benefit, such as improved compliance, that is expected to lead to an improvement in serious outcomes.”¹⁵

Under the Negotiation Program, CMS is required to consider “the extent to which the selected drug and therapeutic alternatives to the drug address unmet clinical needs”. The CMS definition of unmet need is far too narrow to adequately consider conditions that require complex treatments and for which there are different possibilities for positive clinical outcomes. A more robust definition will ensure that CMS is not undervaluing the patient perspective. There are many reasons patients may believe that the needs of their community are not met by current treatments and therapeutics. This can include but is not limited to treatments having major side effects, not being totally

¹⁵ U.S. Food and Drug Administration. Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. June 2014. <https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf>

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effective, or adversely interacting with other medications/comorbidities for the patient. To protect patients, this definition must be expanded to align more closely with the needs of the Medicare population. Unmet need cannot mean only that no other treatment options exist. Instead, it must look at the nuanced factors that go into managing, treating, and curing a given condition. **CMS should expand their definition of unmet clinical needs to align with that of the FDA.**

§110: Utilization management and Requirements for Coverage

As noted in the initial guidance, drugs selected for negotiation must be included on Medicare plan formularies. However, the guidance did not provide information regarding the potential use of utilization management (UM) tools, even if selected drugs are required to be included on formularies.

The Negotiation Process will allow the Medicare program to negotiate and accrue per unit savings on the eligible drugs and biologics that accrue the highest annual expenditures. UM tools are most commonly applied to direct beneficiaries through tiered formulary placement or step therapy. However, Medicare's establishment of the MFP by definition indicates that the program is paying a "fair price" for the therapeutic benefit derived from a drug or biologic. In isolation, the utilization-based need for UM techniques should be severely lessened.

At the same time, the IRA included a broader redesign of the Part D program which increases plan liability for drug costs once a beneficiary has reached the annual out-of-pocket limit (\$2,000 in 2025, indexed to growth in Part D expenditures in subsequent years). This change in liability is likely to broadly incentivize increased use of UM tools. This would be problematic, as UM efforts like prior authorization, step therapy, and cost sharing lead to increased patient and administrative burden, worse long-term outcomes, stress, costly out-of-pocket expenses, and an inability for a patient to work with their care provider to determine the best course of treatment. This would be problematic, as

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UM efforts like step therapy and cost sharing through placement on non-preferred formulary tiers leads to increased patient and administrative burden, worse long-term outcomes, costly out-of-pocket expenses, and an inability for a patient to work with their care provider to determine the best course of treatment.


The Alliance encourages CMS to provide guidance directing MA-PD and PDP plans to limit or avoid use of UM for drugs selected for negotiation. It is currently unclear if and how negotiation may impact patient access. However, incentives to increase use of UM may confound the access impacts of negotiation with impacts of Part D redesign. By prohibiting plans from using step therapy or placing drugs selected for negotiation on non-preferred or specialty formulary tiers, CMS can better observe changes in access as a result of these policies. Further, beneficiaries should be able to broadly access drugs for which the cost as established through the MFN is reflective of therapeutic benefit.

Contact Information

The Alliance thanks CMS for the opportunity to comment on this issue. If you have any questions or would like to follow up on the items discussed in our comments, please contact Adina Lasser, Public Policy Manager, at alasser@agingresearch.org. We look forward to continuing our work with you on this issue.



Michael Ward
*Vice President of Government Relations
and Government Affairs*



Adina Lasser
Manager of Public Policy



April 14, 2023

The Honorable Chiquita Brooks-LaSure
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC

Re: Medicare Drug Price Negotiation Program Initial Guidance

Dear Administrator Brooks-LaSure:

On behalf of the Alliance for Patient Access (AfPA), thank you for the opportunity to comment on the initial guidance implementing the Medicare drug price negotiation program. As CMS continues the implementation process, we urge you to continue to engage patients and providers during the process, address the potential usage of new or additional utilization management tools on these negotiated treatments and continue to examine and evaluate how current guidance affects innovation, especially for rare diseases treated by orphan drugs.

About AfPA

Founded in 2006, AfPA is a national network of policy-minded health care providers who advocate for patient-centered care. AfPA supports health policies that reinforce clinical decision making, promote personalized care and protect the clinician-patient relationship. Motivated by these principles, AfPA members participate in clinician working groups, advocacy initiatives, stakeholder coalitions and the creation of educational materials.

Patient and Provider Perspective

CMS is correct to seek input from a broad range of stakeholders to ensure this new authority fairly and accurately meets the needs of interested stakeholders. Patient and provider voices are crucial to this process, providing feedback that can only be obtained through lived experience, either with prescribing the treatments being negotiated under the proposed guidance or using them. It is important to combine real-world experience with data and information gathered via engagement with manufacturers and insurers. Patients who live with the conditions treated using the negotiated medications can provide information on patient benefits. Health care providers who treat these conditions can provide their perspective on how IRA implementation could limit their ability to treat these conditions and unintended consequences regarding the clinician-patient relationship.

To ensure optimal care, it is critical that providers can utilize every tool in their toolbox, and patients can access timely, personalized care. We encourage CMS to engage patients and providers in implementation discussions throughout the process to ensure proposed guidance does not limit access to care.

This comment period for the initial guidance is a great opportunity for patients and providers to provide perspective on how CMS should implement this authority, but further opportunities should be built into future rulemaking and guidance. We ask CMS to prioritize finding ways to engage these crucial voices in the process, whether it is through written comment and opportunities such as town halls or public roundtables.

Patient Access – Utilization Management

The goal of this program is to reduce costs to the federal government by negotiating drug prices, which we are appreciative of. Patients pay significant money for their treatments and all solutions to bring down patient costs should be thoroughly examined. However, we urge CMS to ensure that patients still retain access to these medications, even after the prices have been negotiated.

We'd like to thank CMS for requiring Part D plans to cover the negotiated treatments; however, initial guidance has not yet addressed the use of utilization management techniques or patient cost-sharing tactics, commonly used by insurers to limit access to treatments. These tools can include long prior authorization processes and step therapy protocols. When utilization management tools are implemented, patient access to the treatment prescribed by their clinician is delayed or denied. These delays can lead to worsening conditions, new, potentially dangerous side-effects, and higher downstream medical costs.

We urge CMS to explicitly address these tactics and make clear that negotiated drugs cannot be subjected to onerous utilization management requirements. Doing so would help ensure patients can continue to access timely, appropriate care. Patients should have clear access to all covered medications and CMS should ensure that insurance providers do not limit access to negotiated treatments.

Quality Adjusted Life Year

The Inflation Reduction Act (IRA) prohibits CMS from using the quality-adjusted life year (QALY) in setting prices. This is critical as the QALY is an artificial valuation metric that discriminates against patients with chronic conditions, older beneficiaries and patients living with disabilities. While the outright use of the QALY to determine value is prohibited, we are concerned that implicit usage of the QALY could still find its way to the process. We urge CMS to ban the use of the QALY, either explicitly, or implicitly via mediums such as studies that utilize the QALY in their methodology or referencing countries, such as Canada, that use the QALY when reviewing medications. The QALY restricts access to medications for some of the most vulnerable patients and should not be used in this process.

Orphan Drugs

The federal government has instituted laws and regulations to encourage innovation for conditions that do not have adequate treatment options available to them. Some of the most needed breakthroughs have occurred in the orphan drug space. Orphan conditions are defined as rare diseases that affect less than 200,000 people in the United States. Federal policy encouraging innovation has led to breakthroughs for many of these conditions, but to ensure new drug discovery continues for patients living with rare diseases, it is important to ensure that these new regulations do not halt progress that has been made to find treatments for these conditions. The IRA does recognize this by prohibiting CMS from requiring negotiation for a treatment that is indicated for only one rare disease; however, CMS has indicated that this exception will only apply to medications indicated for a single rare disease, meaning that a medication indicated for multiple rare diseases could be subjected to negotiations. This could limit rare disease treatment development and innovation as manufacturers often continue research to see if a therapy can treat other diseases. For rare diseases, CMS should consider the unintended consequence that this limited exception could have on continued research and work to ensure that therapies approved for orphan/rare diseases are excluded from negotiations.

Conclusion

We understand the difficult and sensitive nature of drug pricing reform for CMS and appreciate the work being done to ensure that patients can afford their medications. We urge CMS to work to include the patient and provider perspective in each step of the process to ensure patients and health care providers do not face

unintended consequences related to access and future innovation. Specifically, we ask CMS to actively engage the patient and provider community for input on potential consequences of the guidance, ensure that utilization management cannot be instituted for treatments chosen to be negotiated, and protect a clear path to development of orphan drugs throughout this process. We recognize the complexity of the issues facing CMS, and we thank you for allowing the opportunity to comment. If you have questions or would like further information, please contact the Alliance for Patient Access at (202) 951-7097.

Sincerely,

A handwritten signature in cursive script, reading "Josie Cooper". The signature is written in a dark ink and is positioned above the printed name and title.

Josie Cooper
Executive Director
Alliance for Patient Access



April 14, 2023

Re: *Medicare Drug Price Negotiation Program Guidance*

Submitted via email to: IRAREbateandNegotiation@cms.hhs.gov

Dear Sir or Madam,

Thank you for the opportunity to provide comments on the initial guidance memorandum regarding implementation of the Medicare Drug Price Negotiation Program.

The Alliance for Safe Biologic Medicines (ASBM) is a diverse group of stakeholders that includes physicians, pharmacists, patient advocates, researchers, and biopharmaceutical manufacturers. Since 2010, ASBM has worked closely with regulators worldwide as they develop and implement health policies, to ensure that these reflect the best interests of patients. To that end, we have surveyed thousands of physicians in 15 countries; and presented findings to regulators including the U.S. Food and Drug Administration (FDA), the World Health Organization (WHO), the Australian Therapeutic Goods Administration (TGA), Health Canada, the European Commission, the Italian and Spanish Ministries of Health, and others. We also regularly share with policymakers the perspectives of patient advocacy organizations which comprise the bulk of our membership.

ASBM supports policies which increase patient access to affordable, innovative medicines. We further believe that the perspectives of physicians and patients should be given particular weight during this process. Based on these principles, ASBM offers the following comments on CMS' initial guidance for the Inflation Reduction Act's Medicare Drug Price Negotiation Program.

A. Medicare Part D: A Highly Successful Program with a High Satisfaction Rate

Prior to my role as ASBM's Executive Director, I served for 6 years in the Department of Health and Human Services' Office of the Secretary, during which time Medicare Part D (prescription drug benefit) was developed and implemented. The idea of 'negotiation' was raised, evaluated, and rejected during the development of Part D due to numerous factors; among them were the negative impact on innovation and patient access to new drugs.

A recent survey of seniors enrolled in a Medicare Part D plan revealed a 90% satisfaction rate with the program—the highest rate since annual polling began 7 years ago. This high satisfaction rate is based on the program being user-friendly and affordable; over 85% of seniors surveyed claim affordable monthly premiums and co-pays.¹

B. Historical Impact of Price Controls on Innovation and Patient Access

¹ <https://www.hlc.org/post/medicare-part-d-the-successes-and-the-challenges/>

In European countries and Canada, government-negotiated drug pricing (ie, price controls) have negatively impacted patients by undermining innovation and limiting patient access:

- In the 1970s, European companies developed most new drugs; however, since the implementation of price controls in Europe, 60% of new drugs are currently developed in the US, compared to 13% in Switzerland, 8% in the United Kingdom (UK), and 6% in Germany and France.¹
- Of cancer medicines launched globally between 2011 and 2019, more than 96% are available to US patients while only 65% are available in other developed nations such as Australia, Japan and the UK.² Furthermore, cancer death rates per 100,000 are 1.6 to 1.8 times higher in Europe than those in the US.³
- Of new cancer medications, 90% are available to US patients within the first year of launch, whereas less than half of these are available to cancer patients in Germany, the UK, France, and Canada.⁴

Current US policy contributes to the availability of more life-saving medicines, earlier access to new drug launches, and fewer cancer-related deaths.

C. Negative Impact on Development and Adoption of Biosimilars

ASBM seeks to ensure that patients have access to safe biologic treatment options, including lower-cost biosimilar versions of innovator biologics. Market competition (between innovator products and multiple biosimilars to that product) has proven to be an effective means of reducing costs, both in the European Union and in the U.S.

For example, the cumulative savings in drug spend for classes with biosimilar competition is estimated to have been \$21 billion over the past 6 years. Trends show an acceleration in savings per quarter, and in Q2 2022 alone, savings in drug spend due to biosimilar competition were estimated at \$3.2 billion. As these products compete for market share, the average sales price (ASP) of biologics (both reference products and biosimilars) is declining. The prices of biosimilars have decreased at a negative compound annual growth rate (CAGR) of -9% to -24%; the prices of most reference products have decreased at a negative CAGR of -4% to -21%.^{8 5}

Despite these successes, the MFP statute threatens to undermine this market. Rather than providing clarity with its draft guidance, CMS has created more uncertainty. It is particularly concerning that CMS issued final policy for Sec. 30 without any opportunity for stakeholders to comment on the “pause” (“Special Rule”) provisions which will have a major impact on the biosimilars sector. In addition, it imposes a new, subjective standard of “bona fide” marketing of a biosimilar before a reference product may be removed from the selected drug list in Sec. 70 of the guidance.

¹ “Europe negotiates a poor vaccine rollout”; *Forbes*, April 2021

² IQVIA Analytics, FDA, EMA, PMDA, and TGA data. New active substances approved by at least one of these regulatory agencies and first launched in any country from January 1, 2011 to December 31, 2019; June 2020.

³ “Democrat plan on drug costs will stifle innovation”, *San Antonio Express-News*, May 12, 2021

⁴ IQVIA Analytics, FDA, EMA, PMDA, TGA, & w3 Health Canada data, April 2021.

⁵ 2022 Biosimilar Trends Report, Amgen

D. Limitations on Stakeholder Input

Implementation of the Medicare Drug Price Negotiation Program will not follow typical timelines as in the case of other major health care legislation. Under the Inflation Reduction Act (IRA), CMS will implement policy changes via ‘program instruction or other forms of program guidance’ rather than traditional notice-and-comment rulemaking.

CMS has required stakeholders to submit comments on the guidance within 30 days of the March 15, 2023 memorandum (by April 14, 2023); the notice-and-comment period of the Administrative Procedure Act or the Medicare Act is typically longer for complex legislation. ASBM believes that the shortened comment period limits the ability of patients and other stakeholders to provide meaningful input on the guidance. Furthermore, CMS is only seeking input on select portions of the guidance and is not soliciting comments on provisions that are considered ‘final.’ ASBM believes that some of these ‘final’ provisions, such as those related to selection of drugs for price setting and biosimilars are key issues upon which stakeholders deserve an opportunity to comment. For example, Congress has specified that drugs must reach a certain age (9 or 13 years post-launch) before they are subject to maximum fair price (MFP) setting. CMS has finalized (without accepting comments) a policy that will include innovative drugs that have not yet reached the requirements for time on market that are outlined in the IRA.

E. Process Pitfalls

Stakeholders will have limited visibility on how CMS negotiates the MFPs for selected medicines. As outlined in the guidance, the only point of engagement for patients and physicians is via an information collection request (ICR)—a process typically used for technical data collection under the Paperwork Reduction Act.

MFP price setting will be based on therapeutic reference pricing. This standard often fails to consider patient subgroups and preferences, as many alternative therapies do not fit within broad judgments of clinical similarity. In addition, referencing price reporting metrics used by other government agencies (eg, the US Department of Veterans Affairs) are inappropriate benchmarks for care delivered in a community setting, as these procurement prices are intended for special populations receiving care in closed health care delivery systems.

Furthermore, CMS proposes a narrow definition of ‘unmet’ need when setting prices, including only diseases for which there are limited or no treatment options. ASBM believes that defining unmet need in this way will devalue medicines that address important patient needs and will reinforce, rather than reduce, expected harm to progress against unmet need.

F. Impact of CMS Guidance on Innovation

ASBM believes that CMS’ guidance negatively impacts continued innovation by setting rules that will devalue existing patents or exclusivities for selected drugs. Specifically, the Agency intends to consider the length of the available patents and exclusivities and may consider adjusting the preliminary price downward if the patents and exclusivities will last for a number of years. This policy could penalize companies for having secured

patent rights prior to FDA approval (particularly for small molecules) but would be especially damaging for post-approval research and development (R&D).

The R&D that happens after initial FDA approval, including costly and labor-intensive clinical trials, results in innovations that improve patients' lives. Post-approval research is vital, particularly for disease areas like cancer. More than 60% of oncology medicines approved a decade ago went on to receive additional approvals—70% of which occurred seven or more years after initial approval and required significant investment in research and development on the part of the manufacturer. These new uses can provide treatment options for different diseases or patient populations (e.g., pediatric populations). With the policies defined in the IRA guidance, manufacturers will have to reconsider whether post-approval research is feasible in terms of time and resources. They must also consider the impact of a lower MFP if they have obtained patents or exclusivities for these post-approval indications.

ASBM believes that the CMS guidance increases uncertainty for the future of the emerging biosimilars market. Biosimilars play an important role in bringing lower-cost therapies to patients and have provided \$21 billion in savings over the last six years. While Congress enacted a 'Special Rule' enabling certain biosimilar manufacturers to request a delay in the selection and price setting for certain reference biological products, the timelines and criteria imposed to obtain this 'pause' may offer insufficient predictability for biologic and biosimilar manufacturers in the marketplace.

CMS' guidance states that the biosimilar delay will not be available when patent litigation between the biosimilar and reference product manufacturers is ongoing, even if there is a high likelihood that a biosimilar will be approved and marketed under the required timeframes. For example, there may be a settlement for certain dosage forms or strengths, or a biosimilar may elect to market at risk. Nevertheless, CMS would find active litigation 'determinative' that a delay should not be granted.

The MFP initial guidance also does not adequately describe how CMS will protect continued R&D of medicines that help reduce barriers to care for medically underserved communities or meaningfully engage those communities in its decision-making.

ASBM believes that CMS' determination of price for selected drugs may disincentivize innovation in areas that help improve equitable access to care, including for small molecule medicines. A 30-day window to submit data on a selected drug (including whether it meets an unmet need) may not be sufficient to obtain the perspectives of underserved communities with fewer resources. Consequently, this would lead to the inclusion of skewed evidence that does not reflect inputs from diverse and underrepresented groups, such as value assessments conducted by the Institute for Clinical and Economic Review.

G. Implications for Patient Access

While the Part D redesign will help patients by establishing a cap on out-of-pocket spending, government price setting under the IRA could significantly impact patients' access to medicines in Medicare Part D. Specifically, price setting for one selected drug could impact other therapeutic competitors in the same class of medicines. In some cases, Part D plans could force patients to switch from medicines that they have been stable on for months or years. Numerous studies have found that switching stable



patients to a new medicine for non-clinical reasons leads to increased side effects and non-adherence and is often associated with negative health outcomes.

ASBM fears that the downstream effects of broad government price setting will ultimately reduce consumers' choice of plans and formularies in Part D—aspects considered to be hallmarks of the program. As more medicines are subject to MFP over time, the factors that differentiate plans from one another will likely decrease, leading to fewer choices for patients.

In summary, ASBM advocates for policies that ensure the affordability and accessibility of medications and actively promote the paramount importance of patient safety. We believe that government policies that impact patient safety and access to medicines should be transparent, value the input of stakeholders, and incentivize innovation.

ASBM thanks you for the opportunity to provide comments.

Sincerely,

Michael S. Reilly, Esq.
Executive Director
Alliance for Safe Biologic Medicines

ASBM Steering Committee Members:

Alliance for Patient Access
American Academy of Dermatology
American Autoimmune Related Diseases Association
Association of Clinical Research Organizations
Colon Cancer Alliance
Global Colon Cancer Association
Global Healthy Living Foundation
Health HIV
International Cancer Advocacy Network
Kidney Cancer Association
Lupus and Allied Diseases Association, Inc.
National Hispanic Medical Association
National Psoriasis Foundation
ZeroCancer

April 13, 2023

Submitted Via Electronic Filing

*The Honorable Meena Seshamani, M.D., Ph.D.
Deputy Administrator, Centers for Medicare and Medicaid Services
Director, Center for Medicare
Department of Health and Human Services
ATTN: Medicare Drug Price Negotiation Program Guidance
7500 Security Blvd.
Baltimore, MD 21244-1850*

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Deputy Administrator and Director Seshamani:

Alnylam Pharmaceuticals, Inc. (Alnylam) thanks the Centers for Medicare & Medicaid Services (CMS) for this opportunity to comment on the Initial Memorandum regarding the Medicare Drug Price Negotiation Program ('initial guidance')¹.

Alnylam has led the translation of RNA interference (RNAi) from a Nobel Prize-winning discovery into a new class of innovative medicines with the potential to transform the lives of patients who have limited or inadequate treatment options. Our pioneering work delivered the world's first approved RNAi therapeutic with ONPATTRO® (patisiran) in 2018, and we are pleased to have five Food & Drug Administration (FDA)-approved products on the market today that are marketed by Alnylam or other partners. Alnylam also has a deep pipeline of investigational RNAi therapeutics focused on addressing the unmet needs of patients across the following strategic therapeutic areas: genetic medicines, cardio-metabolic diseases, infectious diseases, and central nervous system and ocular diseases.

Alnylam appreciates this opportunity to comment on the initial guidance on the Medicare Drug Price Negotiation Program (MDPNP). As a member of the Biotechnology Innovation Organization (BIO) trade association, we express our broad support of BIO's comments on the guidance. In particular, we echo BIO's recommendations regarding the ways in which CMS can support orphan drug research and development (R&D) and commercialization as it implements the MDPNP. In addition, we underscore the importance of transparency in the negotiations process for drug manufacturers. We urge the agency to implement a predictable and transparent negotiations process, which will help to support continued innovation in the biopharmaceutical industry. We have provided additional comments below related to the support of orphan drug development and commercialization, the agency's consideration of therapeutic alternatives, and the incorporation of level of innovation and

¹ CMS. Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments. 15 March 2023.

investment into the agency's assessment of a Maximum Fair Price (MFP). We hope these comments will be useful to CMS in its implementation of the MDPNP.

1. Alnylam strongly encourages CMS to utilize its existing authority to minimize the impact of the MDPNP on orphan drug innovation.

Congress recognized the importance of supporting access to treatments for patients with rare disease by establishing a protection for certain orphan drugs within the MDPNP of the Inflation Reduction Act (IRA) of 2022.² Specifically, drugs for which there is only one orphan designation and for which the approved indication (or indications) is associated with that designated rare disease or condition are exempted from Medicare drug price negotiations. In creating this exemption, Congress also acknowledged the difficulties drug manufacturers must overcome with respect to the unique scientific, clinical, and commercial challenges of developing transformational rare disease drugs.

Unfortunately, the specifics of the orphan drug exemption mean that the protection will be confined to a narrow set of orphan medicines. This narrowness calls into question the extent to which innovation in rare disease development will be unharmed by Medicare drug price negotiations. Alnylam is concerned that, absent broader protections for orphan medicines – particularly drugs with multiple orphan-only indications – Medicare negotiations could discourage companies from pursuing new indications for existing rare disease drugs or developing rare disease drugs altogether. A meaningful portion of orphan drugs ultimately obtain multiple orphan indications to treat multiple rare conditions; a recent report found that as of 2019, 25% of orphan drugs had multiple orphan designations. The narrow exemption within the IRA undermines existing incentives and protections for orphan drug development, and undermines manufacturers' abilities to investigate new applications for existing therapies.³ In fact, since the passage of the IRA, multiple companies, including Alnylam, have announced changes to their clinical development pipeline plans in light of the narrowness of the orphan drug exemption, highlighting the real-world impact that the legislation is already having on orphan drug R&D and investment.^{4,5}

Alnylam is appreciative that, in its initial guidance, CMS is “considering whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development.” We strongly encourage the agency to utilize its current authority to mitigate against any unintended consequences from negotiations on the development of new treatments for rare diseases. Specifically, we urge the agency to clarify that, where an orphan drug loses eligibility for the orphan drug exclusion, the seven-

² 117th Congress (2021-2022). H.R.5376 - Inflation Reduction Act of 2022. Public Law No: 117-169.

³ Orphan Drugs in the United States: Rare Disease Innovation and Cost Trends Through 2019. IQVIA & the National Organization for Rare Disorders. December 2020, *accessible at* <https://rarediseases.org/wp-content/uploads/2022/10/orphan-drugs-in-the-united-states-NRD-2020.pdf>.

⁴ Grogan, J. The Inflation Reduction Act Is Already Killing Potential Cures. Wall Street Journal. 3 November 2022, *accessible at* https://www.wsj.com/articles/the-inflation-reduction-act-killing-potential-cures-pharmaceutical-companies-treatment-patients-drugs-prescriptions-ira-manufacturers-11667508291?reflink=desktopwebshare_permalink.

⁵ Alnylam Pharmaceuticals Form 10-K Annual Report for the Fiscal Year Ended 31 December 2022, *accessible at* <https://www.sec.gov/ix?doc=/Archives/edgar/data/1178670/000117867023000005/alny-20221231.htm>.

or eleven-year “qualified single source drug” clock runs from the date on which the drug lost eligibility for the exclusion. Additionally, as many orphan medicines are molecules with multiple orphan-only indications – and therefore are not currently protected from Medicare negotiations – we strongly urge the agency to apply a different standard when considering therapeutic alternatives for such orphan medicines to take into account the advancements in innovation which have enabled novel approaches to targeting rare diseases, including targeting the underlying genetic basis for disease.

We thank CMS for considering these recommendations and any additional actions in order to ensure the orphan drug exclusion is maximally protective of rare disease therapy development, commercialization, and access.

2. Alnylam requests that CMS carefully consider the level of innovation and assess whether true therapeutic alternatives exist for a selected drug when determining an MFP to protect incentives for American scientific innovation.

In its initial guidance, CMS has established a qualitative approach to form its ongoing “preliminary price” offer. The approach is founded on referencing the net prices / average sales prices (ASPs) of therapeutic alternatives treating the same indication in order to establish a “starting point,” which is then adjusted based on the agency’s assessment of clinical benefit compared to its therapeutic alternatives. The agency acknowledges that multiple methods for establishing the starting point were evaluated, including using production and distribution costs, the statutory ceiling price, a domestic reference price, a “fair profit” price based on R&D or production and distribution costs, or the net prices / ASPs of therapeutic alternatives. The approach based on therapeutic alternatives was the only method which allowed CMS to take the cost of other treatment options into account when assessing the clinical benefit of a selected drug.

Alnylam is concerned that by basing the starting point for a preliminary price on net prices / ASPs of therapeutic alternatives, and by taking a broad approach to the set of therapies which might be considered viable therapeutic alternatives for comparison, CMS risks undermining the importance of and incentives for innovation in the research and development of new treatments, particularly for rare, debilitating and often-fatal diseases. As proposed, the selection of therapeutic alternatives does not currently account for innovation, and allows for highly innovative drugs to be compared to older, less-advanced therapies. Many emerging technologies represent a dramatic advancement over existing therapeutic alternatives. For instance, Alnylam’s RNAi technology has provided a novel mechanism of action with the potential to halt – or even reverse – disease progression in certain disease areas where other treatments cannot. A method that uses existing alternatives as a starting point for price negotiation fails to accurately reflect the value of a selected drug which might have a significantly improved delivery profile, safety profile, or a demonstration of outcomes relative to drugs identified as potential therapeutic alternatives.

It is crucial that CMS continue to foster technological advancements even in categories where therapeutic alternatives may exist. Setting a starting point price for negotiations

based on a therapeutic alternative regardless of the alternative's level of innovation risks comparing truly novel therapeutic advances against therapies which predate important scientific advances in a particular disease area. The risk of drawing such a comparison for the purposes of setting an MFP may result in a negotiated price which does not reflect the value provided by an innovative drug, and as a result is likely to disincentivize highly meaningful new developments for patients, as noted above, particularly in categories where there are or may be upcoming therapeutic alternatives – even if there is significant room for improvement in terms of delivery, safety, and outcomes.

Alnylam is further concerned that the agency proposes an overly broad scope of literature review to identify therapeutic alternatives. Given the diversity of the US population and specific needs of the Medicare population, broadening the scope of literature review beyond peer-reviewed research involving one or more US-based investigators to include data submitted by the public may lead to the consideration of drugs whose status as viable therapeutic alternatives is not adequately supported by available evidence, as real-world prescribing practices (as reflected in public data submissions) may often deviate from evidence-based standards.⁶ Similarly, the inclusion of studies conducted exclusively by investigators outside the United States may result in inappropriate consideration of drugs that are not used in clinical practice in the indication of interest (and are therefore not true therapeutic alternatives) in the United States.

In addition, we are concerned that the data and other considerations CMS will consider to establish the MFP as part of its flexible process do not sufficiently take into account the level of innovation offered by a selected drug. The absence of explicit consideration of the level of innovation possessed by a selected drug risks inconsistent application of, and insufficient accounting for, the value of innovation in the assessment process, and risks the selection of an MFP which fails to fully account for the value offered by an innovative therapy.

In summary, Alnylam urges CMS to reconsider its approach to selecting therapeutic alternatives for selected drugs, and to take selected drugs' levels of innovation into account when drawing comparisons to existing treatments. It is of utmost importance that the MDPNP preserves the ecosystem and protects the incentives which foster new healthcare innovations for patients in need.

3. Alnylam urges CMS to account for the extensive high-risk investments needed to bring new medicines to patients in identifying a drug's MFP.

Research and development in the biopharmaceutical industry are highly time- and resource-intensive and entail a great deal of risk. The process of bringing a new therapy to market, particularly one which is highly innovative, often takes many years and also entails a high rate of failure in order to achieve success. At Alnylam, we have invested over twenty years and have raised over \$7.7 billion to fund our efforts to create a new therapeutic class

⁶ Chin et al. Heart Fail Rev. 2016;21:675–697.

based on ribonucleic acid (RNA) interference using Nobel Prize-winning technology.⁷ Our first commercial product, ONPATTRO® (patisiran), was approved in 2018 after sixteen years of R&D, and at the time it was the first and only approved treatment in the U.S. for the polyneuropathy of hATTR amyloidosis in adults and the first approved RNAi therapy. hATTR amyloidosis is a multisystem, rapidly progressive, often fatal disease that impacts approximately fifty thousand patients worldwide.

The investment made by Alnylam to create an innovative new class of medicines was significant, and it is not unique. In general, it is estimated that each newly approved drug takes over ten to fifteen years and costs over \$1-2 billion on average to develop.⁸ This substantial outlay of time and capital resource is impacted in part by the high degree of resources attributed to the over 90% of drug candidates which fail prior to entering clinical studies or during phase I, II, or III trials or approval.^{9,10,11}

In its passage of the IRA, Congress directed CMS to consider R&D spending and recoupment of direct and indirect costs as a factor to determine a selected drug's negotiated price. Alnylam is concerned that the implementation of the R&D spending factor, as currently proposed, does not account for the other significant investments required to achieve approval and marketed status of a selected drug. There are an increasing number of drugs today which are generated by platform technologies, like Alnylam's RNAi class of medicines. Indeed, Congress has recognized the potential of platform technologies to speed access to therapies when it passed the Food and Drug Omnibus Reform Act (FDORA) of 2022, with the goal of promoting a more efficient, streamlined pathway to innovative new therapies.¹² The resources required upfront to support platform R&D are significant, with further innovations needed over time to improve the platform to support the development of multiple, new therapies. As such, Alnylam is particularly concerned that the language in CMS's initial guidance does not appear to take into account spending on innovation, such as the resources required to build a platform technology, which can be applied to multiple drugs, or drugs which never achieve marketed status.

The agency's current framing of how it will consider R&D costs for the purposes of the MDPNP appears to be too limited and not aligned with how biopharmaceutical organizations or investors account for R&D costs in practice. Neglecting the investments made on the over 90% of drug candidates which fail to reach approval could lead to significant under-valuing of drugs in the negotiation process. This could have drastic implications for patient access to medicines, especially in areas of high unmet need. We therefore urge CMS to consider a more holistic view of R&D costs among the other

⁷ Maraganore, J. Reflections on Alnylam. *Nat Biotechnol*, 2022;40:641–650. doi: 10.1038/s41587-022-01304-3

⁸ Hinkson I.V., Madej B., Stahlberg E.A. Accelerating therapeutics for opportunities in medicine: a paradigm shift in drug discovery. *Front Pharmacol*. 2020;11:770.

⁹ Dowden H., Munro J. Trends in clinical success rates and therapeutic focus. *Nat Rev Drug Discov*. 2019;18:495–496.

¹⁰ Takebe T., Imai R., Ono S. The current status of drug discovery and development as originated in United States academia: the influence of industrial and academic collaboration on drug discovery and development. *Clinical and translational science*. 2018;11:597–606.

¹¹ Sun D., Gao W., Hu H., Zhou S. Why 90% of clinical drug development fails and how to improve it? *Acta Pharm Sin B*. 2022 Jul;12(7):3049-3062. doi: 10.1016/j.apsb.2022.02.002. PMID: 35865092; PMCID: PMC9293739.

¹² 117th Congress (2021-2022). H.R.2617 - Food and Drug Omnibus Reform Act of 2022, signed into law as part of the Consolidated Appropriations Act, 2023. Public Law No: 117-328.

considerations informing their ingoing offers to negotiating with manufacturers. Incorporating a broader set of R&D costs will better account for the high-level of risk the biotechnology industry and its investment partners assume to bring new medicines to patients.

* * *

In summary, Alnylam supports the comments offered by our trade organization, BIO. Additionally, we encourage CMS to take any possible actions to better support the development of important new orphan drugs. We call on CMS to ensure that therapeutic alternatives are identified and evaluated in an appropriate manner, and that the level of innovation offered by a selected drug is adequately considered and accounted for to protect existing incentives for American scientific innovation. Finally, we urge CMS to reframe their consideration of R&D costs to account for the extensive high-risk investments the biotechnology and pharmaceutical industries are required to make in order to bring new medicines to patients.

We greatly appreciate the opportunity to comment on this initial guidance. Should you have any questions, please do not hesitate to contact me at dparsons@alnylam.com.

Regards,



Deirdre Parsons
Senior Director, Global Public Policy & Government Relations
Alnylam Pharmaceuticals, Inc.



April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services
200 Independence Avenue S.W.
Washington, D.C., 20201

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator LaSure:

The American Cancer Society Cancer Action Network (ACS CAN) is making cancer a top priority for public officials and candidates at the federal, state, and local levels. ACS CAN empowers advocates across the country to make their voices heard and influence evidence-based public policy change, as well as legislative and regulatory solutions, which will reduce the cancer burden. As the American Cancer Society's nonprofit, nonpartisan advocacy affiliate, ACS CAN is more determined than ever to end cancer as we know it, for everyone.

As CMS implements Medicare drug price negotiation, ACS CAN offers recommendations to ensure Medicare beneficiaries realize the full potential of this new program. Every Medicare beneficiary is either a cancer patient, survivor, or at risk of developing the disease and the affordability and availability of cancer prevention, early detection, treatment, and survivorship is critical to reducing the significant nationwide cancer burden.

Drug therapies play an integral role in cancer treatment and survival. Both cancer patients and survivors rely on medications to treat their cancer and prevent recurrence. Over the course of the last few years there has been a remarkable increase in the number of new cancer drug therapies. In 2022 alone, 10 out of the 37 new drug therapies approved by the Food and Drug Administration (FDA) were for cancer.¹

Advances in research have significantly improved our understanding of cancer at the molecular level – leading to the development of more precise detection and diagnostic tools and the corresponding therapies that can attack cancer. However, if patients likely to benefit from these advancements face barriers of affordability or accessibility, the opportunity to reach the national goal of eliminating death and suffering

¹U.S Food and Drug Administration, New Drug Therapy Approvals 2022, <https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/new-drug-therapy-approvals-2022>.

from cancer is greatly hindered. Access to a full range of prescription drug therapies is, therefore, a key determinant in successful cancer outcomes.

The affordability of cancer therapies, however, remains a serious obstacle for many cancer patients. Even with Medicare coverage, beneficiaries who need access to innovative cancer drugs may find their out-of-pocket costs running into thousands of dollars each year. For those battling cancer, skipping pills, or abandoning prescribed drug therapies because of cost can have serious health consequences. Other patients go into significant debt, even bankruptcy, to pay for their treatments.²

The newly enacted cap on Medicare Part D out-of-pocket drug costs will help to make prescription drugs more affordable. As CMS begins to negotiate lower prices for select drugs in Medicare, there is the potential for further savings for millions of beneficiaries if the program is administered in a manner to ensure that access to new and innovative therapies is protected and savings directly reach beneficiaries, not just overall savings for the program. Given historical Medicare spending data, it is highly likely that cancer drugs will account for a substantial proportion of the drugs to be negotiated. If this is the case, it is even more critical that CMS consider the many unique oncology considerations to ensure critical therapies and future innovation is not impeded.

ACS CAN appreciates the opportunity to comment on the initial program memoranda. We offer some general recommendations for ensuring that patients benefit the most out of the negotiations as well as specific comments in direct response to questions CMS has raised in different sections of the draft.

The Importance of Patient Guardrails

ACS CAN views affordability and access as equally critical for ensuring that cancer patients receive the best treatment to survive their disease. As CMS moves forward with implementation of the new prescription drug negotiation program, we urge you to carefully balance the need to lower the cost of drugs offered through Medicare with ensuring patient access to new drug therapies. To this end, ACS CAN asks you to consider several patient “guardrails” that could help to achieve that goal.

Monitoring and Reporting

ACS CAN encourages CMS to carefully monitor and publicly report on the implementation of the negotiation process as it pertains to beneficiary access and cost, specifically:

- We urge CMS to ensure that Medicare enrollees realize the savings related to drugs that are the subject of negotiation and in no case pay more out-of-pocket for a drug that is subject to negotiation than they were paying previously. Absent clear directive from CMS, a drug that is subject to negotiation could be placed on a higher formulary tier (for example, a non-preferred brand) and enrollees could pay higher cost-sharing as a result.
- As CMS identifies the drugs subject to negotiation, we urge the Agency to determine whether a particular disease (like cancer) represents a majority of drugs subject to negotiation. If a majority of

² Liz Szabo, “Sticker Shock Forces Thousands Of Cancer Patients To Skip Drugs, Skimp On Treatment”, Kaiser Health News, March 15, 2017, <https://khn.org/news/sticker-shock-forces-thousands-of-cancer-patients-to-skip-drugs-skimp-on-treatment/view/republish/>.

drugs subject to negotiation pertain to one disease or condition, CMS should consider (as part of the factors related to negotiation) the impact on long-term research, investment, and unique characteristics of innovation for that disease. For example, drugs with a single orphan designation are exempt from negotiation, but the protection is not extended to products with multiple orphan designations. This seems to provide a powerful disincentive for drug sponsors to explore new, lifesaving uses in rare diseases, of which most cancers are, for drugs already proven safe and effective.

- While the guidance document pertains to the Medicare negotiation process for Part D covered drugs and the guidance related to Part B drugs is forthcoming, we also recognize that CMS has a vested interest in adopting similar rules pertaining to both programs (in order to reduce administrative complexity for both the program, manufacturers, and plans). Therefore, we urge CMS to monitor the prescribing patterns of drugs subject to negotiation to determine whether prescribing patterns are generally on trend after the negotiation process. If prescribing patterns fall beyond a statistically significant measure, we urge CMS to conduct independent analysis to determine why prescribing has changed. This may be more of an issue with respect to Part B negotiation given the direct impact of physician reimbursement, but we recommend that CMS put in place monitoring processes for both programs to ensure beneficiary access.

Review the Potential for Steering

CMS should monitor plan formularies to determine the extent to which plans are using more utilization management tools for non-negotiated drugs, which can hinder access to these medications. ACS CAN is concerned about the extent to which beneficiaries could be steered towards negotiated drugs. For cancer patients who have found a specific drug that works for treating their cancer, being steered towards another – potentially less effective drug – could be detrimental. Medicare Part D is administered entirely through private plans which have a financial incentive to steer beneficiaries toward a drug with the lowest price the plan is able to negotiate. To the extent that providers have a choice of drugs to prescribe (e.g., several drugs available in the same therapeutic category and class) the Part D plan could steer beneficiaries toward the negotiated drug and may impose barriers (such as more rigorous prior authorization or step therapy requirements) on non-negotiated drugs.

Examine Impact on Launch Prices

CMS should examine any potential increase in launch prices as a result of negotiation and the overall impact on beneficiary costs and determine the extent to which higher launch prices potentially negate some of the potential beneficiary savings from negotiation. CMS should monitor and publicly report this information as part of the transparency of the Medicare negotiation process. This will help inform stakeholders as they seek to make refinements through the program, some of which may require Congressional action.

Monitoring Access Issues

Cancer is not just one disease it is hundreds of diseases. As such, there are many FDA-approved cancer drugs that are used for cancers not indicated in the formal label. According to the Agency for Healthcare Research and Quality (AHRQ) one in five prescriptions written today are for off-label use.³ There is a statutory recognition of the appropriateness of such prescribing by covering oncology drugs for off-label use when

³ Agency for Healthcare Research and Quality. Off-label drugs: What you need to know. Available at <https://www.ahrq.gov/patients-consumers/patient-involvement/off-label-drug-usage.html#:~:text=Off%2Dlabel%20prescribing%20is%20when,are%20for%20off%2Dlabel%20use> .

included in a recognized compendia.⁴ Given this important feature of oncology drug use, CMS should consider not only the FDA-approved label indication of the drug but also the extent to which the drug is prescribed as an off-label use for another cancer. If the negotiation process unintentionally results in barriers to accessing medications (e.g., overuse of utilization management tools) or prescribing changes, there is a concern that beneficiary access to non-negotiated drugs may be negatively impacted. Therefore, CMS should begin to monitor any potential beneficiary access problems to establish a baseline for future comparison.

Examine Impact on Research and Development of New Therapies

While the overall cancer mortality rate continues to decline, there is still enormous unmet need for the development of therapies to treat cancer. Because the creation of negotiation processes will have downstream impact on research and development, we encourage CMS to work closely with the FDA, particularly on issues related to the trends in the number of new cancer therapies brought to market.

Specifically, we ask CMS to closely monitor two provisions that may negatively impact research and development of new therapies - the implications on research of additional indications for new therapies and the impact on the development of small-molecule therapies since they are eligible for negotiation after only seven years on the market.

Many oncology medicines approved a decade ago also received approvals for additional indications in later years, and most of those were seven or more years after initial FDA approval. Often times these indications are for earlier stage cancers when cancer is more treatable, and many expanded indications are for rare cancers. We ask CMS to work with the FDA to monitor and report on the implications of this new price negotiation program on the submission of applications for new indications of existing therapies and to identify negative trends.

Small-molecule oral oncology drugs are very important tools in the treatment of cancer. These therapies can be taken by patients at home, which can reduce patient time and transportation burdens. We ask CMS to work with FDA to monitor the implications of this new price negotiation program on the submission of applications for small molecule therapies.

Future Revisions to the Negotiation Process

We recognize that given the statutory deadlines, CMS was not able to obtain stakeholder input regarding the Medicare Part D negotiation process through rulemaking and instead is implementing the program through guidance. We thank the Agency for its willingness to release the draft guidance and for solicitation of stakeholder input.

At the same time, we recognize that the negotiation process is new to the Medicare Part D program and there are bound to be opportunities for improvements to the program moving forward. CMS should consider undergoing rulemaking in future years to formalize the negotiation process. CMS could also use this process to establish a timeline by which the Agency intends to revisit the rules regarding the negotiation process. Using the rulemaking authority will provide stakeholders clear direction regarding the process for negotiation and will ensure an open and transparent process for any subsequent changes to the negotiation process.

⁴ 42 U.S.C. §§13952w-102(e)(4).

Recommendations on Specific Sections of the Memoranda

CMS is soliciting comments on specific issues raised in the memoranda. ACS CAN offers the following comments and recommendations in response to some of the questions CMS raised.

Section 50.2 – Evidence about Therapeutic Alternatives for the Selected Drug

To determine the maximum fair price of a selected drug CMS is required by law to consider evidence about alternative treatments including the comparative effectiveness of the selected drug and therapeutic alternatives, and the effects of the selected drug and its therapeutic alternatives on specific populations (including individuals with disabilities, the elderly, the terminally ill, children, and other patient populations). CMS is prohibited from using comparative clinical effectiveness research – including quality-adjusted life years (QALYs) in a way “that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.”

ACS CAN supports comparative effectiveness research because it provides clinicians with information regarding the relative clinical effectiveness of a given intervention and potential differences in side effects. We appreciate CMS clearly stating that it will “not use evidence in a manner that treats extending the life of any individual as lower value than the life of another individual; this includes QALYs when used in association with life extension.”

ACS CAN strongly opposes the use of quality-adjusted life years to determine whether to provide coverage or to set patient cost-sharing for a given treatment. Doing so fails to consider the value an individual may place on the quality of life provided to them for a given treatment. ACS CAN believes that cancer treatments should be patient-centered and ensure a patient’s preferences in treatments and outcomes.

Section 60.3.3.1 – Analysis for Selected Drugs with Therapeutic Alternatives

To compare the effectiveness and clinical benefit between a selected drug and its therapeutic alternatives, CMS indicates it intends to:

- Identify outcomes to evaluate for each indication of the selected drug, and consider the safety profile of the selected drug and the therapeutic alternative;
- Consider health outcomes, intermediate outcomes, surrogate endpoints, patient-reported outcomes, and patient experience;
- Focus the review of clinical benefit on outcomes of particular importance to the condition or disease being treated by the selected drug;
- Consider the effects on specific populations, as required by section 1194(e)(2)(C);
- Consider if the selected drug fills an unmet medical need; and
- Examine improvements in outcomes with the selected drug as compared to its therapeutic alternative to determine whether a selected drug represents a therapeutic advance.

We remind CMS that in oncology, there are very few drugs that are truly equivalent with respect to the FDA-approved label indication and the scientific evidence supporting the efficacy of a given drug. For example, both Keytruda and Opdivo are FDA-approved to treat lung cancer, but the efficacy of both drugs is not the same across all patients with lung cancer. Lung cancer itself is not a single disease but is subdivided into small-cell lung cancer and non-small cell lung cancer, which is further defined by up to 10 distinct biomarker-driven subtypes. We urge CMS to consider the real-world use of a particular medication across all types and subtypes of a disease for purposes of determining whether a drug has a therapeutic alternative.

ACS CAN supports the use of both patient-reported outcomes and patient experience data. Patients have first-hand knowledge of the effectiveness of a treatment as well as the impact on quality of life. We also support CMS considering health outcomes such as cure, survival, progression-free survival, or improved morbidity when comparing the selected drug to therapeutic alternatives. We support CMS considering whether a selected drug fills an unmet medical need such as treating a disease or condition in cases where extremely limited or no other treatment options exist as this is particularly important for cancer patients.

Section 60.7 – Exclusions from Negotiation Process

Under the new law, negotiation is delayed for those drugs where there is a high likelihood that a biosimilar will be licensed and marketed in the next two years.

ACS CAN has long supported the appropriate use of generic drugs and has been a staunch supporter of bringing more biosimilars to market. This is another way of both expanding options for cancer patients and lowering costs for their drugs. While outside the direct scope of implementing the new negotiation program, ACS CAN urges CMS to work with FDA to expedite approval of generics and biosimilars.

Section 90.2 – Monitoring Access to the MFP

ACS CAN supports CMS' intent to require Primary Manufacturers to establish safeguards to ensure information about the maximum fair price for selected drugs is available to eligible individuals, pharmacies, mail order services, and other dispensers. Program transparency and, in this case, price transparency will be key to overall success of the negotiation program.

We support the proposal for CMS to publish the information on its website and recommend that it be done in an easy to read, easy to access, consumer-friendly format. We also recommend that CMS update the Medicare Plan Finder with information for those drugs that are subject to Medicare negotiation. In reviewing Part D plan formularies, CMS should ensure that enrollees' cost sharing is based on the Medicare negotiated rate. We further suggest CMS consider other avenues consumers generally use to get information on coverage including:

- the Medicare toll free line and call center;
- insurance plan websites;
- pharmacies and pharmacy applications;
- patient navigators; and
- patient advocacy organizations.

We support CMS' proposal to establish a process by which beneficiaries can report violations. This system should be easy to use – such as a toll-free number or an online notification system – and widely publicized. We urge CMS to set a time limit – no more than 48 hours – for responding to beneficiaries reporting violations and guidance as to the steps they should take. CMS should also report the number of complaints it receives and the number of complaints which resulted in CMS action. Finally, we urge CMS to consider creating an Ombudsman that serves as a direct point of contact for beneficiaries.

Conclusion

ACS CAN appreciates the opportunity to comment on the implementation of the new prescription drug negotiation program. If you have any questions or need additional information, please feel free to contact me directly or Kirsten Sloan, Managing Director, Public Policy at Kirsten.Sloan@cancer.org.

Sincerely,

A handwritten signature in black ink, appearing to read "Lisa A. Lacasse". The signature is fluid and cursive, with the first name "Lisa" being the most prominent.

Lisa A. Lacasse, MBA
President
American Cancer Society Cancer Action Network

April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services
Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244

Submitted electronically

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Brooks-LaSure,

The American College of Rheumatology (ACR), representing over 7,700 rheumatologists and rheumatology interprofessional team members, appreciates the opportunity to provide thoughts on the Medicare Drug Price Negotiation guidance that was released on March 15, 2023. We recognize that establishing this complex program is a tremendous undertaking and appreciate all opportunities for the public to participate in the process.

Rheumatologists and rheumatology healthcare professionals provide ongoing care for Medicare beneficiaries with complex chronic and acute conditions that require specialized expertise. They provide primarily non-procedure-based care to patients with severe conditions that can be difficult to diagnose and treat, including rheumatoid arthritis and other forms of inflammatory arthritis, vasculitis, systemic lupus erythematosus, and multiple other debilitating diseases. Rheumatologists and rheumatology professionals work side by side with pharmacists and PharmD's to ensure patients' access to medically necessary therapy. Early and appropriate treatment by rheumatologists and rheumatology professionals can control disease activity and prevent or slow disease progression, improve patient outcomes, and reduce the need for costly surgical or interventional procedures. The improved outcome enables our patients to continue to be more productive than they would have been without timely treatment.

Therapeutics for rheumatic diseases are as complex as the diseases they treat, and we recognize the tremendous investment in research and development that is needed to bring these innovative drugs and biologics to market. However, R&D costs do not account for soaring drug prices – prices that routinely block patients' access to medically necessary therapies. The ACR believes that, in order to allow patients access to needed treatments, all participants in the pharmaceutical marketplace, not just manufacturers, must be called upon to improve transparency, address perverse incentives, incentivize world-class innovation in drug development as well as reliable manufacturing and distribution systems, and reduce the cost borne by patients to levels that no longer preclude access to medically necessary therapy.

Ensuring Accessibility and Innovation

The ACR recognizes that this guidance outlines technical steps that will allow the agency to negotiate select drug prices with manufacturers. The drug negotiation provisions within the Inflation Reduction Act (IRA) require an aggressive timeline in order to meet the 2026 applicability deadline. We note that an aggressive timeline could lead to unintended consequences in that a relatively short interval between approval by the Food and Drug Administration (FDA) of a drug and its listing on the drug pricing negotiation list could disincentivize manufacturers from investing in new and innovative therapies. Therefore, as CMS continues to refine the program, we urge the agency to ensure that the drug pricing timeline and eligibility requirements allow for high-spend drugs to be negotiated without prejudicing innovation.

Provider and Patient Perspective

As prescribers, we sit at the nexus between innovative therapies and the patients who would benefit if they could afford them. This unique perspective will be invaluable to the successful rollout of CMS's evolving policies. Therefore, we urge CMS to ensure appropriate stakeholder and public participation, including 60- or 90-day comment periods and the inclusion of patient and provider perspectives throughout the process. Incorporating patient and provider real-world perspectives as the end-users of these products is integral to any plan to reduce drug prices.

We encourage CMS to make negotiation methodologies transparent, accessible, and understandable to all stakeholders. Along these lines, we urge CMS to publish all subsequent policies related to this program in line with the customary regulatory process, including an adequate comment period.

Finally, we urge CMS to include patient and provider groups, including the ACR, throughout the program's development. While the negotiations toward a maximum fair price are largely between the pharmaceutical industry and CMS, the implications of these negotiations are far-reaching. We appreciate that the agency recognizes the need for quarterly strategic and stakeholder meetings. We urge CMS to be candid and transparent in these discussions and allow for additional mechanisms, including listening sessions, by which others might participate to ensure the program meets all objectives and mitigates unintended consequences.

The ACR appreciates the transparency CMS has provided in the early stages of the implementation of the negotiation program. We urge continued transparency and more time for input from stakeholders. The ACR welcomes all opportunities to serve as a resource to CMS as drug negotiations begin. Please do not hesitate to contact Amanda Grimm Wiegrefe, MScHSRA, Director of Regulatory Affairs, at awiegrefe@rheumatology.org should you have any questions or need clarification.

Sincerely,

A handwritten signature in black ink, appearing to read "D. White".

Douglas White, MD, PhD
President, American College of Rheumatology



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April 14, 2023

VIA ELECTRONIC DELIVERY

IRARebateandNegotiation@cms.hhs.gov

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Brooks-LaSure:

Amgen Inc. (Amgen) appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year (IPAY) 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

Amgen is committed to using science and innovation to dramatically improve people's lives, improving access to drugs and biologics (collectively, "drugs," consistent with CMS's convention), and promoting high-quality care for patients. Amgen develops innovator medicines and biosimilar biological products. Thus, our interest is to ensure a robust market for, and improve patient access in the United States to both innovator and biosimilar biological products.

We are pleased to provide CMS with feedback on certain aspects of the implementation of the Drug Price Negotiation Program. However, Amgen remains concerned that the government price controls on certain medicines provided through Medicare under the guise of price "negotiation" under the Inflation Reduction Act (IRA) is likely to stymie biopharmaceutical innovation at precisely the time when the world needs more new medicines to treat an aging population. Government price setting provisions are forcing biopharmaceutical companies to make hard



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choices when it comes to research and development (R&D) investment. Companies are having to rethink how and where they invest in medical innovation, with the government essentially picking winners and losers by discouraging the development of some types of medicines and treatments for certain patient populations.

Biopharmaceutical innovation is key to addressing long term sustainability of health systems (e.g., prevention and avoided acute events in the future because of prevention efforts), improving public health and people's lives. We encourage CMS to consider the impact to innovation, including for biosimilars and the improved affordability options these medicines offer, and patient access as the agency considers guidance for this and other IRA-related programs.

Amgen also supports the comments of the Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Innovation Organization (BIO) on the Drug Price Negotiation Program Guidance.



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I. AMGEN HAS SIGNIFICANT CONCERNS WITH SECTION 30, BUT CMS HAS NOT PERMITTED COMMENT

Although Amgen appreciates the opportunity to submit comments on several aspects of the Drug Price Negotiation Program Guidance, Amgen is troubled by the statement in the Guidance that CMS need not accept comments on Section 30. Section 30 of the Drug Price Negotiation Program Guidance addresses several key aspects of the Program, including CMS's plan to implement portions of the statute permitting CMS to delay, under certain circumstances, selection of a reference biologic for inclusion in the Drug Price Negotiation Program. Even if CMS could permissibly implement these policies without public input, CMS should not do so.

To the contrary, Amgen believes that the uninformed execution of Section 30 will have negative and unintended consequences. As one example, in Section 30.3.1 of the guidance, CMS interprets Section 1192(f) of the Social Security Act (SSA), which establishes a Special Rule that permits CMS to delay selection of a reference biologic for price setting for up to two years under certain circumstances. But in so doing, CMS actually has created a framework that will erect significant barriers to biosimilars ever reaching patients, because the timelines established in Section 30.3.1 will create uncertainty for would-be biosimilar manufacturers and depress incentive for development. If given the opportunity to comment on Section 30, Amgen would have submitted comments to: 1) help CMS understand the challenges posed to biosimilar manufacturers by section 30.3.1 and 2) propose solutions to these problems. Amgen is disappointed to not be given a chance to voice its perspective on these issues and to work with CMS in order to avoid a dramatically negative impact on the biosimilars market.

II. RECOMMENDATIONS REGARDING INCLUSION AND REMOVAL OF PRODUCTS FROM THE MAXIMUM FAIR PRICE (MFP) PROGRAM

A. CMS Must Abandon Its Extra-Statutory and Ill-Advised Bona Fide Marketing Standard (Section 90.4)

With respect to the "bona fide marketing" standard under Section 90.4 of the guidance,¹ there is no statutory basis for CMS's proposal "to monitor whether robust and meaningful competition exists in the market once it makes such a determination [that a generic drug or biosimilar biological product has been marketed]."² The National Drug Code (NDC) Directory published and

¹ Note that we are commenting only on the discussion of "bona fide marketing" under section 90.4 of the guidance. If CMS had permitted comment on section 30, Amgen would have submitted comments on the discussion of "bona fide marketing" in section 30.1.

² Drug Price Negotiation Program Guidance § 90.4.



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maintained by the Food and Drug Administration (FDA) includes the “start marketing date” and “end marketing date” for NDCs and these dates in the NDC Directory should be the beginning and end of CMS’s inquiry.

First and foremost, the agency’s proposed standard is incompatible with the clear language of the statute. By definition, marketing means “[t]he act[] . . . of bringing or sending a product or commodity to market.”³ Thus, once a product has been bought or sold, it has been marketed. CMS does not have the discretion to interpret this statutory term otherwise. Notably, CMS proposes a definition of “marketing” that is consistent with law in Appendix C of the guidance, proposing to define the term as “the introduction or delivery for introduction into interstate commerce of a drug product.”⁴

The statute contemplates that a selected drug will exit the program based on such a determination but does not provide CMS a role in monitoring generic and biosimilar competition.

Any monitoring by CMS of the competitive landscape for pharmaceuticals would duplicate the existing efforts of the Federal Trade Commission (FTC), which has the statutory authority and expertise to perform this function. It is also unnecessary in light of FDA initiatives, including the Drug Competition Action Plan⁵ and Biosimilars Action Plan,⁶ which have focused on improving access to generic and biosimilar products in the U.S. Moreover, the FTC and FDA have been working together on these issues releasing joint statements and holding joint workshops, most recently focusing on competition for biologics and biosimilars.⁷ CMS also lacks the expertise and resources to police marketplace competition issues. CMS’ proposed monitoring of the status of competition in the marketplace is therefore unauthorized and unnecessary.

Notably, the subjectivity of the standard provides the agency with boundless discretion in implementing the program, a circumstance Congress clearly did not intend. Take the Maximum Fair Price (MFP) termination date: Congress expressly defined that date by reference to the date

³ Oxford English Dictionary, Definition of Marketing, <https://www.oed.com/view/Entry/114186?rskey=36dfg4&result=2&isAdvanced=false#eid> (last visited Mar. 19, 2023).

⁴ Drug Price Negotiation Program Guidance Appendix C.

⁵ FDA Drug Competition Action Plan, available at <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/fda-drug-competition-action-plan> (last accessed Apr. 13, 2023).

⁶ FDA Biosimilars Action Plan: Balancing Competition and Innovation, available at <https://www.fda.gov/media/114574/download> (last accessed Apr. 13, 2023).

⁷ FDA and FTC Collaborate to Advance Competition in the Biologic Marketplace, available at <https://www.fda.gov/news-events/fda-voices/fda-and-ftc-collaborate-advance-competition-biologic-marketplace>.



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on which CMS determines that a generic or biosimilar has been marketed.⁸ Yet, for no justifiable reason, CMS has indicated that such date does not similarly trigger the termination of the IRA's MFP liability. In doing so, the agency purports to vest itself with limitless discretion to determine the MFP termination date, based on its subjective judgment. Similarly, the agency has implicitly asserted the power to, after an MFP has been terminated, *re-institute* an MFP should the agency conclude that utilization of the generic or biosimilar is no longer "robust and meaningful"⁹—again, an entirely subjective standard.

There is no indication, in the text or structure of the statute, that Congress intended to give CMS such sweeping authority. To the contrary, CMS's action is patently unlawful, in light of the clear statutory boundary imposed by the objective, point-in-time date of marketing standard. "It is axiomatic that an administrative agency's power to promulgate legislative regulations is limited to the authority delegated by Congress. Thus, if there is no statute conferring authority, a federal agency has none."¹⁰ Yet through its bona fide marketing standard, CMS is "effectively [seeking to] introduce a whole new regime of regulation," which "is not the one that Congress established."¹¹ No statute has conferred authority to implement such a regime.

Another significant concern is the agency's apparent assumption that widespread utilization of a new generic or biosimilar will occur overnight. In actuality, there will inevitably be a ramp-up period for a newly launched product, not only because there is a lag before sales are reflected in claims data, but also because there is a period during which providers and patients transition to a new product.¹² This is especially true for biosimilars, given that it can take months or years for newly launched biosimilars to gain traction in the marketplace. But, by any rational understanding, the product is in fact marketed during this transition period. The existence of a period before Prescription Drug Event (PDE) data reflect widespread utilization should not preclude a finding that a generic or biosimilar has been marketed. CMS's proposed approach also fails to account for circumstances where there is not "robust and meaningful competition" on account of an unexpected shortage or supply chain concern.

B. CMS Should Remove a Drug from the Selected Drug List After the "Negotiation Period," But Before an MFP is in Effect (Section 70)

⁸ SSA § 1192(c)(2).

⁹ See Drug Price Negotiation Program Guidance § 90.4.

¹⁰ *Michigan v. EPA*, 268 F.3d 1075, 1081 (D.C. Cir. 2001).

¹¹ *MCI Telecomms. Corp. v. Am. Tel. & Tel. Co.*, 512 U.S. 218, 114 (1994).

¹² See A. Lubby, Factors Affecting the Uptake of New Medicines: A Systematic Literature Review, 14BMC Health Services Research 469 (2014) (describing the various factors that affect early uptake of new medicines).



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We urge CMS to interpret the IRA to allow a reference product to exit the MFP program if a generic or biosimilar product is marketed after the “negotiation period” but before the start of the IPAY. Such reading aligns with the statutory definition of a “qualifying single source drug” (QSSD)—a threshold requirement for a drug to be subject to price setting. The statute defines a QSSD “with respect to an [IPAY],”¹³ indicating that a product’s status as a QSSD must exist as of the first day of the IPAY, not just at the selected drug publication date, as CMS suggests in section 70 of the guidance. Had Congress intended QSSD status to be assessed only as of the selected drug publication date, it would have said so. Thus, a product that has become multisource before the IPAY should not be subjected to price setting.

This view also comports with the definition of “price applicability period,” which means, “*with respect to a qualifying single source drug*, the period beginning with the first IPAY with respect to which such drug is a selected drug and ending with the last year during which the drug is a selected drug.”¹⁴ This reference to QSSD status signals that a product that has gone multisource and hence no longer meets the QSSD definition should not be subject to a price applicability period. Moreover, as the statute and CMS’ Figure 1 show, only products that are QSSDs may be negotiation-eligible drugs. Where a product is no longer a QSSD, it cannot, by definition, be considered a negotiation-eligible drug or a selected drug.¹⁵

Our position aligns with subsection (c)(1) in section 1192 and its use of the phrases, “with respect to an IPAY” and “with respect to such year” in paragraph (1).¹⁶ This phrasing supports the conclusion that negotiation-eligible status (and hence, QSSD status) must remain in place as of January 1 of the IPAY for subsection (c)(1) to apply to the drug. Thus, this provision speaks to the exit process for drugs that remain a QSSD and selected drug on the first day of the IPAY and then experience generic or biosimilar competition. Paragraph (2) provides a “clarification” of the application of paragraph (1) to a specific time period when various tasks otherwise would need to be performed by both CMS and the manufacturer, i.e., during the “negotiation period.” The provision does not address what happens if the generic or biosimilar is marketed after the “negotiation period,” as there is no “negotiation process” to which the manufacturer is subject, and thus no need for a clarification that the process must stop. Paragraph (2)’s styling as a “clarification” shows that the statutory terms referenced in subsection (c) must be given full effect in subsection (c)(1). In other words, it does not change the fact that the statute defines QSSD “with respect to an IPAY.”

This position is grounded in sound policy. Congress crafted the IRA to provide for price setting for *single source* products. CMS’s current position undermines this intent by applying MFPs to

¹³ SSA § 1192(e)(1).

¹⁴ *Id.* § 1191(b)(2) (emphasis added).

¹⁵ *Id.* §§ 1192(c) (defining “selected drug”), 1192(d) (defining “negotiation-eligible drug”).

¹⁶ *Id.* § 1192(c)(1).



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products that are already multisource. This position thereby directly undermines generic and biosimilar competition and incentives for pursuing approval of such products. For generic and biosimilar companies, developing and marketing generic and biosimilar products within the timeframes under the law is already challenging. The processes necessary to market a generic or biosimilar product can be complex, and there are many steps that are not solely in control of the generic or biosimilar sponsor, including FDA review timelines. The price-controlled MFP may go into effect before such companies are ever able to market their products and CMS may set a price below the level of economic viability. CMS's position compounds this problem by essentially providing that generic or biosimilar marketing in the last thirteen months before the IPAY does not trigger exit from the MFP program. In other words, a generic or biosimilar company that brings its products to the market during these thirteen months will nevertheless be forced to compete against a medicine that has its price set with an MFP.

We therefore urge CMS to revise the Drug Price Negotiation Program Guidance to provide that a reference product or listed drug exits the program if generic or biosimilar marketing occurs after the "negotiation period" but before IPAY. CMS also should amend the table on page 63 of the Guidance as follows:

Date on which CMS determines that a generic drug or biosimilar biological product is approved and marketed	Result with respect to selected drug for the Negotiation Program
September 1, 2023 through August 1, 2024 <u>December 31, 2025</u> (which includes Negotiation Period for initial price applicability year 2026)	Selected drug remains a selected drug for initial price applicability year 2026, though MFP does not apply; selected drug ceases to be a selected drug on January 1, 2027
August 2, 2024 <u>January 1, 2026</u> through March 31, 2026	Selected drug remains a selected drug and MFP applies for initial price applicability year 2026; selected drug ceases to be a selected drug on January 1, 2027.
April 1, 2026 through March 31, 2027	Selected drug remains a selected drug and MFP applies for initial price applicability year 2026 and calendar year 2027; selected drug ceases to be a selected drug on January 1, 2028.

III. RECOMMENDATIONS REGARDING THE PRICE SETTING FACTORS



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A. CMS Should Reconsider Information It Requires Manufacturers to Submit under Appendix C (Appendix C)

Section 1194(e)(1) of the SSA lists the following categories of data to be submitted by manufacturers for consideration by CMS in setting the MFP:

- Research and development costs;
- Unit costs of production and distribution;
- Federal financial support for discovery and development;
- Data on certain pending and approved patent applications, exclusivities, and FDA applications or approvals; and
- Market, revenue, and sales volume data in the United States.¹⁷

In Appendix C to the Drug Price Negotiation Program Guidance, CMS proposes definitions of these five categories of information. As discussed further below, Amgen is concerned that it will be impossible or infeasible for manufacturers to produce some of the information described in Appendix C, particularly given the excessive civil monetary penalties (CMPs) that can be imposed for failure to comply. Moreover, other information described in Appendix C is highly sensitive, yet inappropriate and unnecessary for setting the MFP.

1. CMS should limit mandatory disclosures to information necessary to administer the Maximum Fair Price Program

The proposed mandatory submissions described in Appendix C are incredibly broad and burdensome, but it is unclear how CMS intends to use most of the information for price setting. For example, CMS proposes to require manufacturers to report R&D costs broken down by six categories (where, as discussed below, manufacturers are unlikely to track R&D costs in this way). However, under section 60.3.4, CMS appears to be proposing to consider only total R&D costs, stating that it will consider adjusting the initial offer price upward or downward based on whether the manufacturer has recouped its R&D costs. Thus, CMS is proposing to require a burdensome (and, as discussed below, potentially impossible) allocation of R&D costs into six categories with no articulated purpose.

Likewise, CMS proposes to require manufacturers to provide an extensive list of confidential commercial information characterized as “market data and revenue and sales volume data,” yet,

¹⁷ SSA § 1194(e)(1); *see also* Drug Price Negotiation Program Guidance § 60.3.4.



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in section 60.3.4, CMS struggles to explain how it will use this data, other than indicating “if the average commercial net price is lower than the preliminary price, CMS may consider adjusting the preliminary price downward.”¹⁸

Another example is that CMS is proposing to require disclosure of a poorly defined category of information labeled “U.S. commercial average net unit price— best.” Manufacturers already expend significant resources to report “best price” under the Medicaid Drug Rebate Program (MDRP) and CMS provides no rationale as to why it needs manufacturers to calculate and report this additional best price.

CMS also provides no explanation as to why it would mandate disclosure of “quarterly total U.S. unit volume.”¹⁹ As the IRA is a Medicare-only price setting program, it is not obvious why CMS needs manufacturers to report non-Medicare unit volume. Even if one could guess at potential uses for such information, this is sensitive, potentially market-moving information that manufacturers should not be disclosing to CMS without good reason.

Congress did not give CMS carte blanche. Under section 1193(a)(4)(B) of the SSA, CMS may require manufacturers to submit “information that the Secretary requires to carry out” the agency’s price setting activities.²⁰ In order for CMS to be authorized to mandate disclosure of information, CMS must articulate why the agency “requires” such information for the MFP program.

2. CMS should permit manufacturers to adopt reasonable assumptions with respect to manufacturer-submitted information

In lieu of its proposed definitions,²¹ CMS should clarify that, in submitting such information, a manufacturer may make reasonable assumptions when interpreting the statutory terms describing such information.²² In doing so, CMS can rely on existing reasonable assumptions policy, under which manufacturers have long been permitted to operate.²³

¹⁸ Drug Price Negotiation Program Guidance § 60.3.4.

¹⁹ *Id.* at Appendix C.

²⁰ SSA § 1193(a)(4)(B).

²¹ Drug Price Negotiation Program Guidance, Appendix C.

²² See SSA § 1194(e)(1); see also *id.* § 1193(a)(4), 1194(b)(2)(A) (addressing manufacturer information submission obligations).

²³ See, e.g., 83 Fed. Reg. 12,770, 12,785 (Mar. 23, 2018) (providing for an MDRP agreement provision governing reasonable assumptions); 71 Fed. Reg. 69,624, 69,667 (Dec. 1, 2006) (discussing reasonable assumptions regarding ASP reporting). Allowing manufacturers to rely on reasonable assumptions will be particularly important in the early years of the Drug Price Negotiation Program, while CMS and stakeholders are determining how to best implement it. But reliance on reasonable assumptions should be allowed to



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Reasonable assumptions enable manufacturers to adopt an appropriate approach to meeting a legal requirement where law and policy do not specify one. Reasonable assumptions thereby allow manufacturers to meet complex and nuanced legal requirements without requiring Congress or CMS to speak to the unique circumstance of each manufacturer and its product portfolio and business practice. As a result, regulatory regimes can be readily operationalized notwithstanding routine ambiguities in law and policy.

This recommended approach is preferable to the proposed rigidly standardized one across all manufacturers and products notwithstanding the unique characteristics of each of the over 20,000 prescription drug products currently approved for marketing in the United States.²⁴ These products feature diverse histories of development and FDA regulation, chains of ownership, and pricing and sales arrangements in complex drug distribution chains. The proposed rigidly standardized approach would therefore necessarily result in arbitrary treatment of products that would inappropriately advantage some manufacturers and products over others.²⁵ Further, it could result in CMS not receiving information that the manufacturer has concluded is most relevant for consideration in the price setting process.²⁶

3. *CMS should allow manufacturers to submit information maintained in the usual course of business with respect to R&D costs*

continue on an ongoing basis given the complexity of the program and the diverse business realities of manufacturers. Such an approach is consistent with the approach CMS has taken under other new and complex programs. For example, with respect to whether “a self-insured group health plan, a large group market health plan, or a grandfathered group health plan . . . have used a permissible definition of [Essential Health Benefits (EHB)] under . . . the Affordable Care Act,” the Departments of Health and Human Services, Labor, and the Treasury have stated that they “intend to use their enforcement discretion and work with those plans that make a *good faith effort* to apply an authorized definition of EHB to ensure there are no annual or lifetime dollar limits on EHB.” CMS, FAQ on Essential Health Benefits Bulletin, <https://www.cms.gov/ccio/resources/files/downloads/ehb-faq-508.pdf> (last accessed Apr. 4, 2023) (emphasis added).

²⁴ See FDA, Fact Sheet: FDA at a Glance, <https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance#:~:text=There%20are%20over%2020%2C000%20prescription,FDA%2Dapproved%20animal%20drug%20products> (Aug. 17, 2022).

²⁵ See 5 U.S.C. § 706(2)(A).

²⁶ See *generally Motor Vehicle Mfrs. Assn. of United States, Inc. v. State Farm Mut. Automobile Ins. Co.*, 463 U.S. 29, 43 (1983) (agency decision-making must be based on *relevant* data and must consider important aspects of the problem at hand).



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As an initial matter, Amgen joins PhRMA in urging CMS to take a global view to R&D costs and look at the total investments across the entire portfolio, rather than asking manufacturers to produce information at a product-specific level.

If CMS moves forward with mandating disclosure of product-specific information, we ask that it abandon the proposed detailed definition of R&D costs, including the six specific categories listed and permit manufacturers to submit estimates of R&D costs using reasonable allocation methodologies and information maintained in the usual course of business. We are concerned that CMS is under the impression that manufacturers track and maintain R&D cost information at a level of detail that does not correspond with actual business practices. Amgen does not track product-specific R&D costs in the six categories in Appendix C, nor is such tracking a standard industry practice, making it doubtful that any manufacturers track expenses in this manner either. An attempt at compliance would require Amgen to review prior expense records and invoices and retrospectively flag them by product and CMS R&D cost category. It may prove to be an impossible task to assemble and submit accurate information, but, even if did not, it would be immensely time consuming, expensive, and burdensome. It would be even more challenging for older products, such as those subject to the MFP program, and products acquired through merger or acquisition.

In contrast, many manufacturers have developed methodologies for business planning purposes to allocate R&D costs across products, although we are not aware of a uniform industry standard. Permitting manufacturers to submit this information would not only be more feasible, but it likely would provide a more accurate estimate of costs than trying to piece together old expense records and invoices.

4. Acquisition costs allocated to R&D should be included in R&D costs

In the Drug Price Negotiation Program Guidance, CMS proposes that manufacturers not include drug acquisition costs as part of R&D.²⁷ This is an ill-conceived policy that CMS should reverse when it issues its final guidance document. Given that CMS proposes under section 60.3.4 to adjust the initial offer price upward or downward based on whether the manufacturer has recouped R&D costs, it appears that CMS believes that molecules developed in-house should be assigned greater value than products that have been acquired. This distinction makes no business sense. Manufacturers such as Amgen are constantly investing in their internal R&D as well as evaluating opportunities to “buy R&D” through external acquisitions. In either case, the value of the therapy is the same to patients, health care providers, and payers. And the product

²⁷ Drug Price Negotiation Program Guidance, Appendix C; see also Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW) at 5 (Mar. 21, 2023) (ICR).



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may be of greater benefit to patients in the hands of an acquiring company if the company has better capability to market and manufacture a reliable supply of the product. Furthermore, when developing reasonable allocation methodologies related to R&D costs (as discussed above), a manufacturer would never exclude acquisition costs because such an approach would understate, in some cases drastically, the manufacturer's investment.

5. CMS should permit manufacturers to submit a list of patents, exclusivities, and approvals to CMS as part of the initial information request

In the Drug Price Negotiation Program Guidance, CMS proposes to require the submission of "all pending and approved patent applications . . . submitted, sponsored, licensed, and/or acquired" by the manufacturer related to a selected drug, including those that are expired or unexpired, pending or approved, or where the manufacturer is not listed as the assignee/applicant (as for a joint venture).²⁸ In addition, CMS proposes to ask for detailed information on exclusivity periods granted by FDA and all active and pending applications and approvals of the selected drug in which the manufacturer is directly or indirectly involved.²⁹ Given the significant volume of such information, and that such information must be provided only a short time after a drug's selection date (by October 2, 2023, for IPAY 2026 or March 1 of the year that is two years before the IPAY for subsequent IPAYs),³⁰ CMS should permit manufacturers to satisfy this requirement by providing a list of such documentation. CMS would then either be able to access such patent, exclusivity, and application related information via other federal agencies or manufacturers could then provide to CMS requested information related to particular patents, exclusivities, and applications as a supplement to the initial submission of information.

6. CMS should allow manufacturers to submit information maintained in the usual course of business with respect to unit costs of production and distribution

Similar to our comments above with respect to R&D costs, the definitions in Appendix C imagine that costs of production and distribution are tracked in a more uniform, detailed, and product-specific manner than is the case. Accordingly, CMS should permit manufacturers to submit information regarding unit costs of production and distribution using reasonable allocation methodologies that they maintain in the usual course of business.

7. Sales and marketing costs should be included in costs of distribution

²⁸ Drug Price Negotiation Program Guidance, Appendix C; see also ICR at 19-20.

²⁹ *Id.*

³⁰ SSA §§ 1194(b)(2), 1191(d)(5); Drug Price Negotiation Program Guidance § 40.2



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CMS proposes to define current unit costs of production and distribution as expressly excluding marketing costs.³¹ CMS proposes to define marketing “as the introduction or delivery for introduction into interstate commerce of a drug product” but includes a number of such costs that might otherwise be considered marketing costs by this definition in the definition of current unit costs of production and distribution, including packaging, labeling, shipping, operating costs, and production costs.³² CMS thus appears to intend to exclude only sales and marketing costs, such as advertising and related costs, from the definition of current unit costs of production and distribution.

After the FDA approves a product, patients may not see the benefit of it unless manufacturers expend resources to educate health care providers (both disease state education and regarding the safety and efficacy of the product itself), on patient support services, and on staff to negotiate with payers for access to the product. These functions are critical to create awareness of the disease and the product’s efficacy so that the product reaches appropriate patients. Excluding marketing costs creates an inaccurate picture of the full costs of production and distribution related to a product.

8. Patient assistance should not be considered a reduction in net price

In the Drug Price Negotiation Program Guidance, CMS proposes to require manufacturers to submit the U.S. commercial average net unit price (effectively the average net unit price to commercial plans for a selected drug) and the U.S. commercial average net unit price—best (effectively the best price to commercial plans for a selected drug) as part of the market data and revenue and sales volume data.³³ These price types “must be net of discounts, chargebacks or rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, or other price concessions or similar benefits offered by the [manufacturer].”³⁴ CMS should revise these definitions to exclude those transactions, such as coupons and free goods programs, that benefit patients alone, as such transactions, by definition, do not impact any price from the manufacturer to a plan. CMS has recognized this explicitly in its regulatory definition of best price, which excludes transactions with patients where patients alone receive the benefit of the transaction. Where such transactions are excludable from best price, therefore, they necessarily should be excluded from these price types as well.³⁵ These clarifications are essential to ensure both that CMS is relying on pricing

³¹ Drug Price Negotiation Program Guidance, Appendix C; ICR at 15.

³² *Id.*

³³ Drug Price Negotiation Program Guidance, Appendix C; see also ICR at 25-26.

³⁴ *Id.*

³⁵ 42 C.F.R. § 447.505(c)(8)-(12).



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information that is actually representative of prices offered to payers in the course of price setting and to ensure that manufacturers continue to be incentivized to provide savings to patients.

B. CMS Should Not Reduce the Initial Offer Price If R&D Costs Were Recouped (Section 60.3)

As discussed above, under section 60.3.4, CMS proposes to penalize manufacturers that have recouped their R&D costs. This policy is flawed for two primary reasons. First, it does not reflect the reality of how companies consider their R&D investments. Only one of thousands of potential candidates will ultimately result in an FDA-approved medicine, and less than 12 percent of the candidate medicines that make it into Phase I clinical trials are ultimately approved by the FDA.³⁶ Companies account for these odds when they plan their R&D programs, and the revenues from the few successes are utilized to cover the R&D costs of the many failures across their entire portfolio of medicines, not just those in the same therapeutic class or intended mechanism of action. Accordingly, viewing recoupment of R&D costs on a product-by-product basis does not reflect actual business practices of manufacturers.

Second, manufacturers are constantly evaluating opportunities to make R&D more time and cost efficient. For example, Amgen has invested in Complex Innovative Designs (CID) with respect to clinical trials to: 1) make the most efficient use of clinical trial data to simultaneously inform dose selection, generate adequate and well-controlled evidence on efficacy and quality safety data; 2) reduce the probability of inconclusive trials, and enable early and accurate decision-making; and 3) most importantly, shorten the time to bring new therapies to patients. In fact, an Amgen CID program evaluating a potential treatment for Lupus was evaluated favorably by FDA under its CID Paired Meeting Program.³⁷ Under CMS's proposed policy, Amgen's global investment in CIDs would likely not be reporting as a product-specific R&D cost, yet CMS could use the resulting reduction in clinical trial costs to reduce the MFP of an Amgen product. CMS's proposed policy of penalizing manufacturers that recoup R&D costs creates a disincentive for manufacturers to invest in such innovative development initiatives that both reduce R&D costs and get therapies to patients more quickly.

C. CMS Should Disclose the Non-Manufacturer-Submitted Information on Which It Relied in Making an Offer or Responding to a Counteroffer (Section 60.4)

³⁶ Congressional Budget Office, Research and Development in the Pharmaceutical Industry, <https://www.cbo.gov/publication/57126> (last accessed April 14, 2023).

³⁷ CID Case Study: A Study in Patients with Systemic Lupus Erythematosus, available at <https://www.fda.gov/media/155404/download>.



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With respect to *non*-manufacturer-submitted information, CMS should commit to disclosing to the manufacturer any information under section 1194(e)(2) of the SSA, including its sources, on which it relied during the price setting process. CMS suggests that it may discuss this information with manufacturers during negotiation meetings after the rejection of a counteroffer,³⁸ but it is critical that CMS commit to sharing this information at each stage of the price setting process. This commitment is essential to supporting a transparent, informed, and good faith price setting process and is consistent with the intent of the Drug Price Negotiation Program.

Specifically, the statute requires CMS to provide a justification for an initial offer that is “based on” the statutorily specified price setting factors including those described in section 1194(e) (2) of the SSA.³⁹ Congress thus intended for an initial offer to be based on such factors and for this limitation to serve as a meaningful boundary to agency discretion, which it can do only where there is a disclosure to the manufacturer of the information on which CMS relied in making the offer. CMS may not “hid[e] or disguise[e] the information that [it] employ[s]” when developing a rule without committing a “serious procedural error;” and it should not do so here for the same reason.⁴⁰

Such transparency will facilitate a more open dialogue during the price setting process. Just as CMS will have the benefit of information from the manufacturer to inform the agency’s initial offer, the manufacturer will have the benefit of information from CMS to inform any manufacturer counteroffer as well as any manufacturer comment on the agency’s response, creating greater parity between CMS and the manufacturer. Ultimately, this approach will reduce the risk that the MFP is set based on flawed information.

D. CMS Should Specify That It Will Consider All Information Submitted by a Manufacturer in Setting the MFP (Section 60.4)

CMS should specify that it will consider *any* information submitted by the manufacturer in support of the price setting process. The statute does not prohibit the manufacturer from voluntarily submitting *additional* relevant information, beyond the information that the statute requires the manufacturer to submit. And CMS has clear authority to consider *all* information submitted by the manufacturer, whether or not tied to a statutorily specified price setting factors, especially given that the statute does not require the agency to justify a response to a counteroffer based on the statutorily specified price setting factors.

³⁸ Drug Price Negotiation Program Guidance § 60.4.3.

³⁹ SSA § 1194(b)(2)(B).

⁴⁰ *Conn. Light & Power Company*, 673 F.2d 525 (D.C. Cir. 1982). Such transparency will also help CMS meet its obligation to implement a “consistent” negotiation methodology and process by serving as a barrier to irregular decision-making. See SSA § 1194(b)(1).



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E. CMS Should Allow a Manufacturer to Submit Additional Relevant Information as It Arises Throughout the Price Setting Process (Section 40.2)

By statute, a manufacturer of a selected drug must submit certain information to inform the price setting process, including certain information regarding non-Federal Average Manufacturer Price (non-FAMP), R&D costs, production and distribution costs, and revenue and sales volume.⁴¹ CMS has also indicated that it will allow manufacturers to submit evidence about alternative treatments.⁴² This information is due by March 1 of the price setting year (or October 2, 2023, for IPAY 2026), i.e., just one month after the selection date.⁴³ Given the exceedingly short time frame to prepare and submit such information, and the real possibility that new information relevant to the price setting process will become available after the submission deadline, CMS should allow a manufacturer to supplement a timely submission as additional relevant information becomes available or otherwise for good cause—not only during a price setting meeting that takes place after the rejection of a counteroffer, as proposed in the Drug Price Negotiation Program Guidance.⁴⁴

By way of example, new data regarding comparative effectiveness could become available, new therapeutic alternatives could come to the market, manufacturers could face unexpected increases in production costs, or manufacturers could need to restate non-FAMP. It is critical that manufacturers be allowed to submit to CMS the most accurate and up-to-date information related to the market conditions of the selected drug to ensure that the MFP is set as appropriately as possible.

F. CMS Should Abandon the Overly Broad Confidentiality Obligations That It Proposes to Impose on Manufacturers (Section 40.2)

CMS should abandon the overly broad confidentiality obligations that it proposes to impose on manufacturers. These requirements are wholly unreasonable and raise significant legal and policy concerns. We echo PhRMA's concerns and comments.

⁴¹ *Id.* §§ 1193(a)(4), 1194(b)(2)(A), (e)(1).

⁴² CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026, at 2 (Jan. 11, 2023), available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf>; see also SSA § 1194(e)(2).

⁴³ We assume that CMS will designate information under section 1194(e)(1) of the SSA as information that is due by March 1 of the negotiation year (or October 2, 2023, for IPAY 2026) under section 1193(a)(4) of the SSA.

⁴⁴ Drug Price Negotiation Program Guidance § 60.4.3.



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G. CMS Should Establish Clear Rules for Its Price Setting Methodology and Enforcement, Without Using Certain Reference Points (Section 60.3)

CMS should implement detailed standards to enforce a consistent and fair methodology as CMS sets the MFP. We appreciate CMS's inclusion of several criteria, such as reviews of existing literature and real-world evidence, conducting internal analytics, and consulting subject matter and clinical experts within the price setting process. However, related to CMS's methodology overall, it will be essential for CMS to provide clear guidance. CMS should not use reference prices (e.g., "cost-optimized alternative", Federal Supply Schedule (FSS), and Big Four [the Department of Veteran Affairs, Department of Defense, the Public Health Service, and the Coast Guard] pricing) which are contextually incongruous foundations for Medicare and will infallibly undervalue any "therapeutic advance." Given the preliminary phase of the ongoing price setting process, the MFP Program will likely pose a considerable resource burden on CMS and manufacturers, with inevitable uncertainties and shortcomings needing exposure through trial and error. Given all of the uncertainties, ceiling prices should be used for the first several IPAYs until the program has been further refined. CMS should also identify standing exceptions where ceiling prices will be the automatic default (e.g., for indications with high unmet need). Most importantly, CMS's assessment should place greater weight on patient/caregiver impacts rather than expounding a simplistic narrative of manufacturer-driven costs.

H. CMS Should Provide a Methodological Framework that is Predictable, Transparent, and Fair to All Stakeholders (Section 60)

The aim of CMS's framework should be a predictable, transparent, and fair process in setting the MFP that ensures patients have timely and uninterrupted access to innovative medicines and that this innovation is rewarded. Establishing clear definitions for the patient population, intervention, comparator, and outcomes will create a structured framework for stakeholders to provide feedback. In addition, CMS should solicit input directly from clinicians, manufacturers, and professional organizations that adhere to a high standard of methodological excellence. Understanding which patients CMS includes in the MFP assessment from an evidence demonstration perspective will be critical. The identification of an appropriate comparator will also be material to this framework, as any discussion on MFP will be relative to existing treatment options. In addition, CMS will need to clarify the governance of the evidence assessment process and price setting. To ensure transparency and fairness, CMS should specify that the two parts of the process be separated and reviewed independently. Finally, identifying patient-important outcomes as part of the initial framework will ensure the MFP reflects value holistically from the patient's perspective. In short, reaching a consensus on the population, intervention, comparator, and outcomes will be a vital part of the MFP process where stakeholder input is essential.



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It will be difficult for CMS to enforce this clear and consistent framework if its work is outsourced. For the analysis of therapeutic alternatives, CMS should not contract out the research and should exercise caution in even referencing existing value assessments, most of which are inappropriate for the Medicare population, given that they are Quality-Adjusted Life-Years (QALY)-based and geared towards savings for private payers. Likewise, CMS should ensure that all its methodologies are centered on the patient to avoid collaboration with organizations that do not meet these standards.

I. CMS Should Consider a Broad Array of Patient-Centered Outcomes, Including Elements Most Important to Patients, When Assessing “Therapeutic Advance” (Sections 50.2 and 60.2)

CMS should be more specific in its qualifications for a “therapeutic advance”, and this should be informed by a wide variety of outcomes. These should go beyond clinical endpoints to encompass what matters most to patients and the wider care network—outcomes such as productivity, speed of response, caregiver burden, adherence, long-term persistence, scientific spillover, patient choice, and unmet need. CMS needs to consider broader elements of value, such as individual variation in access to care (e.g., physical, financial, and psychological access that could impact health outcomes across different populations), disease heterogeneity (especially when it comes to safety across different patient subgroups), tolerability, co-morbidities, and societal value (e.g., reduced time in long-term care, avoided/prevented acute events, reduced infection rates). Determining relative health benefit based on a broader set of variables ensures all elements of value, not just those critical to payers, are appropriately incorporated into pricing negotiations. We encourage the inclusion of quality of life and patient preference data, and we recognize CMS’s consideration of not using the QALY metric as mandated by statute. We request that CMS exclude other discriminatory metrics incompatible with Section 1194(e)(2), such as life years gained (LYG) and equal value of life years gained (evLYG). LYG only accounts for the quantity, not quality of life, making it largely unhelpful in the economic evaluation of palliative treatments.⁴⁵ EvLYGs place a ceiling cap on all gains in life years and penalize the most innovative therapies that extend life & improve quality of life.⁴⁶

Additionally, the unique characteristics of each therapeutic area and intervention underscore the importance of contextual flexibility. Obtaining additional evidence in both clinical and real-world evidence is often challenging and fraught with inherent limitations and confounders (e.g., placebo effect just by participating in a trial, lower or higher baseline health in studies that make a placebo

⁴⁵ Rand LZ, Melendez-Torres GJ, Kesselheim AS. Alternatives to the quality-adjusted life year: How well do they address common criticisms? *Health Serv Res* [Internet]. 2023;58:433-444, available at <https://onlinelibrary.wiley.com/doi/epdf/10.1111/1475-6773.14116>.

⁴⁶ Basu A, Carlson J, Veenstra D. Health years in total: A new health objective function for cost-effectiveness analysis. *Value Health* [Internet]. 2020; 23(1):96-103



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arm look better, and patients lost to follow-up in a clinical trial or real-world study). When such evidence is submitted, we believe it should be recognized, as it can provide valuable insights into the patient experience and improve patient outcomes. Therefore, we advocate for additional flexibility to enable the inclusion of diverse sources of evidence and facilitate informed decision-making.

J. CMS Should Choose Appropriate Therapeutic Alternatives Based on Clinical Standards, Not Cost (Sections 50.2 and 60.3)

To align best with real-world clinical practice, CMS should select comparators based on widely accepted clinical guidelines, consultation with manufacturers, and reputable resources founded on high-quality evidence. CMS should clearly outline and justify its choice of comparators and align with stakeholders through meaningful outreach. CMS should never select comparators based on price, as this strategy foregoes clinical accuracy to drive down prices artificially.

K. CMS Should Establish and Adhere to a Clearly Defined Hierarchy of Evidence, Which Gives Significant Weight to Real-World Evidence, Indirect Treatment Comparisons, and Broader Measures of Unmet Need (Section 60)

In framing the evidence requirements, CMS should give clear and consistent guidance on how it will assess the evidence. To ensure CMS's analysis is well-rounded and externally valid, we recommend that CMS give significant weight to high-quality, patient-centered real-world evidence (RWE) and provide clear guidance on which RWE it will accept. CMS must also specify how it will weigh data as well as clear conditions under which indirect treatment comparisons are permissible.

CMS also should address how it will consider different types of evidence (e.g., clinical, economic, and humanistic) to arrive at an MFP. While a typical comparative effectiveness analysis considers clinical and safety information, it ignores a broader range of costs and benefits essential to reaching an MFP. For example, caregiver costs and costs associated with lost productivity are huge potential drivers of the value of innovative medicines. It will be necessary for CMS to clearly outline how it intends to formally bring together and weight the various types of data to inform price negotiations.

Contextualizing unmet need is essential to help define comparators, the patient profile (including patient pathways for existing and new drugs), and outcomes. CMS's proposal to limit unmet need to the number of treatment options is too narrow and should expand to consider gaps in health equity, improvements in adherence, and disease areas where treatments exist but quality of life is lacking. In this way, unmet need provides a vital opportunity to quantify disease impact comprehensively (e.g., caregiver burden, productivity losses, intangible costs).



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L. CMS Should Incorporate Meaningful, Transparent, and Predictable Stakeholder Engagement Throughout the Assessment Process (Section 60.4)

Stakeholder engagement is crucial, and CMS should clearly articulate this from the outset. CMS guidance to stakeholders on predictability and transparency in the process and engagement, including adopting a flexible approach, will be essential as its system evolves. At the outset, public announcements on upcoming assessments should be standard, and stakeholders need to be involved in identifying the population, intervention, comparator, and outcomes from an early stage. As the price setting process unfolds, stakeholders must have multiple opportunities for public and private feedback, with sufficient time to respond.

Engagement should be patient-centered, prioritizing the perspectives and needs of patients, their families, and caregivers. Regarding the diversity of Medicare beneficiaries, CMS should work to ensure the translation of complex information for all audiences to understand and engage. Equally, given that different disease populations may include people living with disabilities, CMS should ensure that patients and those in the impacted community can effectively voice their concerns. CMS needs to consider input from a variety of stakeholders carefully and give special consideration to those whom a disease directly impacts. This will help ensure CMS can tailor the engagement process and methodology to the needs of those most affected and will allow CMS to establish a collaborative and inclusive process that promotes trust and transparency. CMS should also commit to reviewing stakeholder engagement not by the number of letters but by how many individuals a given organization represents (e.g., patient advocacy groups or professional medical associations may represent thousands of individuals). Manufacturers should have the opportunity to provide input on other information, alternatives, or comparators put forward by different stakeholders.

IV. RECOMMENDATIONS REGARDING THE PROVISION OF THE MFP (Section 40)

A. CMS Should Finalize Its Proposal Permitting a Manufacturer to Provide Access to the MFP via a Rebate Model and Clarify That the Fourteen-Day Clock for Payment of an MFP Rebate Runs from the Date on Which the Manufacturer Validates Eligibility for the Rebate (Section 40.4)

1. MFP rebate model

Manufacturers must provide the MFP only to:



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- “[T]he pharmacy, mail order service, or other dispenser” with respect to a covered unit of a selected Part D drug dispensed to a [prescription drug plan (PDP)] or [Medicare Advantage Prescription Drug plan (MA-PD)] beneficiary; and
- “[H]ospitals, physicians, and other providers of services and suppliers” with respect to a unit of a selected Part B drug furnished to a Part B or [Medicare Advantage (MA)] beneficiary.⁴⁷

In other words, units of a selected drug subject to MFP pricing may not be dispensed or furnished to MFP-ineligible individuals, e.g., commercial patients.

Yet the statute does not provide manufacturers, or CMS, a right to audit pharmacies and providers to ensure that MFP units were not improperly diverted to MFP-ineligible individuals. And there is no statutory dispute resolution mechanism through which manufacturers can recover MFP discounts from pharmacies and providers that dispensed or furnished MFP units to MFP-ineligible individuals. Indeed, the statute affords CMS no means at all to penalize pharmacies and providers for dispensing or furnishing MFP units to MFP-ineligible individuals.

Given these concerns, we appreciate CMS’s proposal to permit a manufacturer to provide access to the MFP via a rebate model.⁴⁸ Absent CMS enabling an MFP rebate model, as proposed, pharmacies and providers will be free to improperly divert MFP units without any statutory consequence.

*To prevent MFP diversion, CMS should finalize its proposal that access to the MFP may be provided by either “ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP” or “providing retrospective reimbursement for the difference between the dispensing entity’s acquisition cost and the MFP,” i.e., through a rebate.*⁴⁹ The statute does not specify the mechanism by which a manufacturer must provide the MFP. And the statute affords CMS broad discretion to “establish[] . . . procedures to carry out [the Drug Price Negotiation Program], as applicable, with respect to [MFP-eligible individuals].”⁵⁰ The proposed rebate model will enable manufacturers to confirm that a unit was dispensed or furnished to an MFP-eligible individual and therefore is entitled to MFP pricing. The proposed rebate model thus will materially reduce the risk of MFP diversion.

⁴⁷ *Id.* §§ 1191(b)(2), 1193(a)(3). The obligation to provide the MFP to a PDP or MA-PD beneficiary at the point-of-sale is discussed in Section V(D).

⁴⁸ Drug Price Negotiation Program Guidance § 40.4.

⁴⁹ *Id.*

⁵⁰ SSA § 1196(a)(3).



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Notably, the proposed rebate model will not jeopardize Medicare beneficiary access to the MFP-based reduction in cost-sharing.⁵¹ Pharmacies and providers will know at the time a unit of a drug is dispensed or furnished whether a drug is a selected drug and therefore the MFP-based reduction in cost-sharing. Thus, Medicare beneficiaries can readily access MFP-based cost-sharing at the time the unit is dispensed or furnished.

In addition, a rebate model will be familiar to stakeholders given that it is a common model in the commercial sector and under other government programs. The model requires only the minimum Medicare claims data needed to validate eligibility for the MFP and can ensure reasonable time frames for submission of a claim for, and payment of, an MFP rebate.

In contrast, if manufacturers were required to provide the MFP only as an up-front discount at the time of purchase, there would be no mechanism to ensure that an MFP unit is not dispensed or furnished to an MFP-ineligible individual. While a manufacturer or CMS could ask a pharmacy or provider whether an MFP unit was appropriately dispensed or furnished, it would have no statutory recourse if the pharmacy or provider were to refuse to answer or even admit that the MFP unit was improperly diverted to an MFP-ineligible patient. Thus, the MFP that by statute is intended to be provided only with respect to MFP-eligible individuals would effectively be made available with respect to MFP-ineligible individuals too, contrary to the statute's intent.

The 340B Program is generally administered through an up-front discount, but, there, manufacturers at least have a statutory right to audit a 340B covered entity for improper diversion of 340B units as well as a statutory right to subject a dispute to a dispute resolution process.⁵² Moreover, the Health Resources and Services Administration (HRSA), the agency responsible for administering the 340B Program, has statutory authority to audit 340B covered entities and terminate them from the 340B Program for program non-compliance.⁵³ These compliance authorities have not proven sufficient to prevent 340B diversion,⁵⁴ but the Drug Price Negotiation

⁵¹ *Id.* §§ 1847A(b)(1)(B) (providing that Part B reimbursement for a selected drug is based on the MFP such that cost-sharing is based on the MFP as well); 1852(a)(1)(B)(iv)(VII) (specifying that MA cost-sharing for a selected drug may not exceed Part B cost-sharing); 1860D-2(d)(1)(D) (specifying the MFP plus any dispensing fee for a selected drug is the maximum Part D negotiated price, on which cost-sharing is based).

⁵² Public Health Service Act (PHSA) § 340B(a)(5)(C), (d)(3).

⁵³ *Id.*

⁵⁴ For example, the Government Accountability Office (GAO) reports that HRSA typically is not issuing audit findings for diversion consistent with its patient definition guidance on the grounds that it has limited authority to enforce such guidance. GAO, HHS Uses Multiple Mechanisms to Help Ensure Compliance with 340B Requirements (Dec. 2020), available at <https://www.gao.gov/assets/gao-21-107.pdf>. In addition, the GAO has noted that “weaknesses in HRSA’s audit process . . . impede its oversight of covered entities’ compliance with 340B Program requirements at contract pharmacies.” GAO, Drug Discount Program: Federal Oversight of Compliance at 340B Contract Pharmacies Needs Improvement (Jun. 2018), available at <https://www.gao.gov/assets/gao-18-480.pdf>.



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Program does not even provide for such a nominal mechanism, making a rebate model that much more imperative when it comes to preventing MFP diversion.

Congress could not have intended to leave manufacturers and CMS with no means of enforcing the prohibition against MFP diversion. To avoid that perverse result and promote program integrity, we strongly urge CMS to finalize its proposal to permit a manufacturer to provide the MFP via a rebate.

2. Fourteen-day period to pay an MFP rebate

In the Drug Price Negotiation Program Guidance, CMS proposes to give manufacturers fourteen days to provide retrospective reimbursement to providers or pharmacies.⁵⁵ But the agency is silent as to when the fourteen-day clock starts to run. CMS should clarify that the clock runs from the date on which the manufacturer validated that the unit is eligible for an MFP rebate, based on the Medicare claims data submitted by the provider or pharmacy.

If the clock instead were to run from the date on which the provider or pharmacy requested the MFP rebate, it would completely undermine the point of allowing a rebate model. Providers and pharmacies would have no incentive to submit validating data. This approach would be contrary to the intent of Congress, which did not intend to require the MFP to be offered to MFP-ineligible individuals. CMS should clarify that the fourteen-day clock starts only after a manufacturer has validated eligibility for an MFP rebate.⁵⁶

B. CMS Should Adopt an Enforceable Mechanism to Identify 340B-Purchased Units to Prevent MFP/340B Duplicate Discounts Under Medicare Parts B, C, and D (Section 40.4)

The statute prohibits duplicate discounts on MFP-purchased and 340B-purchased drugs. In short, a manufacturer of a selected drug cannot be required to offer both the MFP and the 340B price on the same unit and instead need only offer the lower of these two prices.⁵⁷ It is critical that CMS adopt a mechanism to enable a manufacturer to avoid MFP/340B duplicate discounts— but the Drug Price Negotiation Program Guidance provides for none. In this regard, we support PhRMA's proposal for implementation of one of two different models (the "default payment" or "point of sale" options) to avoid the duplicate discounts that Congress wanted to avoid.

⁵⁵ Drug Price Negotiation Program Guidance § 40.4.

⁵⁶ In the alternative, CMS could specify that a manufacturer must pay an MFP rebate within thirty days of receipt from the provider or pharmacy of all necessary validating Medicare claims data, tolled during the pendency of a reasonable dispute resolution process.

⁵⁷ SSA § 1193(d).



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For drugs reimbursed under Part B, CMS has already established such a mechanism under which, starting January 1, 2024, all 340B covered entities that submit Part B claims must use certain claims modifiers to identify 340B units.⁵⁸

There is no comparable mechanism for Part D drugs or Part B drugs reimbursed under MA. For these drugs, CMS should adopt a mechanism well in advance of the start of IPAY 2026. CMS thus should move quickly to require PDPs, MA-PD plans, and MA plans to identify 340B units of drugs using a consistent identifier in PDE or MA Encounter Data.

CMS recently proposed to require the use of a *Part D* 340B identifier in the course of implementing the Part D inflation rebate program, stating that it “believes that requiring that a 340B indicator be included on the [PDE] record is the most reliable way to identify drugs that are subject to a 340B discount that were dispensed under Medicare part D” for purposes of excluding such units from Part D inflation rebates, as required by statute.⁵⁹ We urge CMS to finalize this proposal.⁶⁰

CMS must also address the need for a 340B identifier with respect to *MA* units of Part B drugs, which is currently unaddressed.

But that is not all. To make the mechanism a meaningful one, CMS should also require the use of a *non-340B* identifier, across Medicare Parts B, C, and D, and specify that a claim for reimbursement for a unit of a selected drug under any such Part is not payable unless the claim is accurately accompanied by either a 340B identifier or a non-340B identifier, as applicable.

Even with an audit right (which does not exist in the Drug Price Negotiation Program), HRSA’s authority and ability to enforce the MDRP/340B duplicate discount prohibition is limited.⁶¹ Thus, the risk of MFP/340B duplicate discounts is real, and CMS must establish a meaningful

⁵⁸ CMS, Part B Inflation Rebate Guidance: Use of the 340B Modifiers (Dec. 20, 2022), *available at* <https://www.cms.gov/files/document/part-b-inflation-rebate-guidance340b-modifierfinal.pdf>.

⁵⁹ CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum 18 (Feb. 9, 2023), *available at* <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>.

⁶⁰ Amgen submitted comments dated March 10, 2023 on this proposal.

⁶¹ For example, GAO reports that HRSA typically is not making audit findings of duplicate discounts “for a failure to follow a state’s Medicaid requirements” on the grounds that it “does not have statutory authority to enforce state Medicaid requirements.” GAO, HHS Uses Multiple Mechanisms to Help Ensure Compliance with 340B Requirements at 15 (Dec. 2020), *available at* <https://www.gao.gov/assets/gao-21-107.pdf>. Compliance with state Medicaid requirements is essential to the MDRP/340B duplicate discount prohibition. See also GAO, Drug Discount Program: Federal Oversight of Compliance at 340B Contract Pharmacies Needs Improvement, GAO-18-480 (2018), *available at* <https://www.gao.gov/assets/gao-18-480.pdf>; see also PHSA § 340B(a)(5)(A).



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mechanism to address this concern and to avoid nullifying the statutory protection against MFP/340B duplicate discounts.⁶² We urge CMS to move quickly to adopt a mechanism that meaningfully prevents MFP/340B duplicate discounts.

C. CMS Should Continue to Recognize That a Manufacturer Cannot Directly Provide Access to the MFP to a Part D Beneficiary at the Point-Of-Sale (Section 40.4)

CMS should continue to recognize that manufacturers cannot provide the MFP on a covered unit of a selected Part D drug to PDP and MA-PD beneficiaries at the point-of-sale *directly*.⁶³ The statute directs manufacturers to provide the MFP on such drugs to such individuals at the point-of-sale in addition to providing it to pharmacies, mail order services, and other dispensers with respect to such individuals.⁶⁴ But Part D enrollee transactions at the point-of-sale are dictated by arrangements between the enrollee, the pharmacy, and the plan or its pharmacy benefit manager (PBM), not by the manufacturer. Manufacturers are not parties to such transactions and do not even enjoy privity of contract with the point-of-sale pharmacy (and sometimes not even with the plan or its PBM).

Thus, we concur with CMS that the MFP must be passed through to Part D enrollees at the point-of-sale by entities that are parties to the point-of-sale transaction.

V. RECOMMENDATIONS REGARDING CIVIL MONETARY PENALTIES (CMPS) (Section 100)

A. CMS Should Establish Procedural Safeguards That Ensure That CMPs Are Imposed Only After Notice and a Reasonable Opportunity to Cure (Section 100)

By statute, CMS may assess significant CMPs if a manufacturer is found to be out of compliance with certain program requirements.⁶⁵ These include penalties of up to \$1 million per day for a

⁶² See *United States v. Markgraf*, 736 F.2d 1179, 1183 (7th Cir. 1984) (“An administrative agency cannot abdicate its responsibility to implement statutory standards under the guise of determining that inaction is the best method of implementation.”).

⁶³ Drug Price Negotiation Program Guidance § 40.4.

⁶⁴ SSA § 1193(a)(3)(A).

⁶⁵ *Id.* § 1197.



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violation of the terms of the negotiation agreement or \$100 million per day for any piece of false information submitted pursuant to the small biotech exception or biosimilar delay provision.⁶⁶

Given the magnitude of these penalties, Amgen supports the imposition of additional safeguards. Specifically, Amgen supports the comments of both PhRMA and BIO in this respect.

VI. OTHER RECOMMENDATIONS

A. CMS Should Establish a Transparent, Predictable, and Reasonable Process for Meaningful Price Setting (Section 60)

By statute, CMS must “develop and use a consistent methodology and process” to negotiate the MFP.⁶⁷ Further, CMS must “specify the process for renegotiation,” which “to the extent practicable, [shall] be consistent with the methodology and process” for initial price setting.⁶⁸

CMS is proposing a price setting process under which CMS would meet with the manufacturer only if the agency rejects a counteroffer.⁶⁹ CMS would then cap the number of meetings at three: the initial meeting and potentially two additional meetings, one requested by the manufacturer and one requested by CMS.⁷⁰

CMS should instead commit to real dialogue throughout the price setting process, without arbitrary limit. This approach is eminently reasonable given that only a limited number of drugs will be negotiated each year.⁷¹ Meaningful price setting requires CMS to engage in continuous manufacturer-specific dialogue, much as a commercial payer would, as opposed to implementing a rote paper-based process. This approach will promote a more transparent and better-informed process for price setting.

CMS’s proposal would defeat this objective by arbitrarily limiting the direct engagement between CMS and the manufacturer to the period after the rejection of a counteroffer—which affords no opportunity for real dialogue at the initial offer stage, which could help the parties avoid any need to consider a counteroffer—and to a maximum of three meetings—which deprives the process of additional insight that the parties may want, which could result in a more informed MFP.

⁶⁶ *Id.* § 1197(a)–(e).

⁶⁷ *Id.* § 1194(b)(1).

⁶⁸ *Id.* § 1194(f)(2), (4)(A), (B). The renegotiation process does not start until 2028. *Id.* § 1194(f)(1).

⁶⁹ Drug Price Negotiation Program Guidance § 60.4.3.

⁷⁰ *Id.*

⁷¹ See SSA § 1192(a)(4).



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Throughout the price setting process, CMS should permit as many meetings as the parties agree would be productive and take meetings before the initial offer stage so that the initial offer is informed by discussions with manufacturers of selected drugs.

VII. RECOMMENDATIONS REGARDING NOTICE AND COMMENT

A. CMS Should Propose and Solicit Comment on the Content of the Agreement It Will Utilize Well in Advance of the Date on Which the First Set of Manufacturers Must Execute the Agreement (Section 40.1)

In the Drug Price Negotiation Program Guidance, CMS commits only to “mak[ing] reasonable efforts to make the final text of the Agreement [that manufacturers must sign for selected drugs under the Drug Price Negotiation Program] available to the public before the selected drug list for IPAY 2026 is published.”⁷² CMS should commit instead to making the content of that document available for public comment before its finalization, and well before the first selection date.

Manufacturers could be subject to CMPs of \$1 million per day for failure to comply with, or even enter into, agreements with CMS regarding prices under the Program.⁷³ Even without these penalties it would be vital to provide manufacturers an opportunity to learn of and comment on the specific terms of the agreement to which they will be subject, before such terms are finalized. Doing so would increase the chances that manufacturers are able to make preparations that will allow them to comply with the agreements. That is particularly crucial here, in light of the significant penalties that may otherwise result. Moreover, “[i]mpossible requirements imposed by an agency are perforce unreasonable” and therefore arbitrary and capricious.⁷⁴ By providing manufacturers notice of and an opportunity to comment on the specific terms of the agreement that CMS intends to impose on them, CMS reduces the chance that manufacturers, deprived of the ability to prepare, will not be able to comply.

B. CMS Should Consider Comments on All Provisions of the Guidance and Respond to Comments on the Guidance in the Final Guidance

⁷² Drug Price Negotiation Program Guidance § 40.1.

⁷³ SSA § 1197(a)–(e); IRC § 5000D(b)(1)(A).

⁷⁴ *All. for Cannabis Therapeutics v. DEA*, 930 F.2d 936, 940 (D.C. Cir. 1991).



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Notwithstanding its previous statement that it would “prioritize transparency and robust engagement” in implementing the Drug Price Negotiation Program,⁷⁵ CMS has taken the position that it need not accept comments on Section 30. As noted above, Amgen has significant concerns about this position, and would have offered comments on Section 30 if permitted to do so.

Beyond Section 30, Amgen asks that, as CMS finalizes its policies, it meaningfully responds to comments received. A comment period is intended “to allow interested members of the public to communicate information, concerns, and criticisms to the agency.”⁷⁶ It is important for an agency to explain how information, concerns, and criticisms raised by stakeholders factored into CMS’s final decision-making so that the comment process can facilitate a “genuine interchange” of ideas between the agency and stakeholders.⁷⁷ Responding to comments helps ensure the agency is considering the full range of points made by the public and helps explain the agency’s reasoning. “The interchange of ideas between the government and its citizenry provides a broader base for intelligent decision-making and promotes greater responsiveness to the needs of the people.”⁷⁸

Responding to comments is particularly important with respect to the Drug Price Negotiation Program given its significant implications for patients, providers, pharmacies, manufacturers, and other stakeholders across the United States. If the agency’s final decision-making is misinformed, barriers to access to essential therapies could result. CMS thus should seek to maximize transparency by meaningfully responding to stakeholder feedback in its final guidance.

* * * * *

We appreciate your consideration of our comments as you develop the Drug Price Negotiation Program policy. Please contact Andrew Swire by telephone at 202-669-6188 or by e-mail at aswire@amgen.com if you have any questions regarding our comments.

Regards,

A handwritten signature in black ink, appearing to read "Greg Portner", is written over a light blue horizontal line.

Greg Portner
Senior Vice President
Global Government Affairs and Policy

⁷⁵ CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026 (Jan. 11, 2023), *available at* <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf>.

⁷⁶ *Conn. Light & Power Co. v. NRC*, 673 F.2d 525, 530 (D.C. Cir. 1982).

⁷⁷ *Id.* (describing the purpose of notice-and-comment rulemaking).

⁷⁸ *Buschmann v. Schweiker*, 676 F.2d 352, 357 (9th Cir. 1982) (internal quotation marks and citations omitted).

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April 12, 2023

Meena Seshamani M.D. Ph.D.
Director, Center for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Dr. Seshamani,

Thank you for inviting comments on the Initial Memorandum on Implementation of Sections 11001 and 11002 of the Inflation Reduction Act. We are pleased to offer the comments set out in what follows. We hope you find them useful in your efforts to implement this important legislation. Our comments are organized to correspond to the outline of the guidance.

Section 30: Identification of Selected Drugs

30. *Definition of a drug for negotiation* Purposes: The Guidance defines a drug as encompassing all products associated with an API. This is a sensible choice. The price of a drug should include all the generic versions in the price estimate. Including the generic version product(s) captures all the volume associated with an API. Failure to do so would overweight brand-name formulations in calculation of the price of a drug.

30.1: CMS should establish a standard that defines the minimum share of the drug at the API level that is subject to generic or biosimilar competition. In small molecule markets with high levels of total spending (over \$500 million) the average generic penetration one year post generic entry is about 65%. Thus, establishing a trigger at 50% to 65% would be based on recent history reflecting the experience of drugs facing true competition from generics.¹ For biosimilar products the initial market shares are considerably lower. Although the evidence is more limited, market shares for biosimilars have been on the order of 20% to 25% a year after entry.² The implication is that if the generic or biosimilar shares of the API fall below the trigger values, the API remains in an uncompetitive market and should remain subject to negotiation.

To estimate generic or biosimilar market share at the API level, a standardized volume measure would need to be applied across dosage forms and strengths. Options include the number of claims (for Part B), standardized prescriptions (for Part D) or defined daily doses. For example, one could

¹ See appendix at the end of the comment for examples of studies offering evidence on this.

² See appendix at the end of the comment.

use Part D claims data to estimate whether more than 50 percent of standardized prescriptions among all the API formulations were dispensed for a generic drug.³

30.1.2 It is not clear if rebates will be incorporated into determining whether a drug has spending below \$200,000,000. Rebates should be included because some drugs have rebates of 80-90% and not including the rebates would yield choices of products that would not reflect true spending by taxpayers.

30.2 *Integration of Rebates Assessment of Spending Exemptions:* It is not clear if rebates will be incorporated into calculations used in the ranking of the 50 negotiation eligible drugs. Footnote 30 attached to point 30 of the guidance suggests that the proposal is to not account for rebates. This works for the selection of the initial 50 negotiation eligible drugs because it makes the data and the selection process transparent. To use rebates in the calculation would disclose rebate data which needs to remain confidential. One possible solution may be that after CMS identifies the top 50 drugs, CMS should exclude any drugs that already have rebates that put their current net price at or close to what would be the maximum fair price ceiling. The statute might provide some flexibility on which one they choose among those that are otherwise eligible.

30.3.1.2 The metrics proposed to assess operational readiness are generally sensible. However, SEC filings about future revenues are nearly always subject to significant caveats around uncertainty and changing market conditions. CMS should consider a more concrete indicator of readiness.

30.3.1.1(3) There is guidance addressing whether there is “bona fide marketing” of the competitor. That review is an important part of the proposal for assessing the legitimacy of potential exclusion of drugs. It could be crafted broadly enough to encompass the type of limited use of a biosimilar as well. It will be necessary to define a “bona fide” competitor. See comment on 30.1 for more information on how to define a “bona fide” competitor.

Section 40: Requirements for Manufacturers of Selected Drugs

40.2 The decision to require the manufacturer to submit data on new and approved NDC-11s or discontinued NDC-11 is appropriate. The provision should ask for the most recent sales for any discontinued NDC-11s.

40.2.2 *Disclosure of Data Used in negotiations and its destruction:* It is not clear what the implications are of an individual engaged in the process disclosing the information to others. The penalties for companies are clear but not for the individuals engaged in the process. People with negotiation information leave companies and the government all the time.

40.2.3 If sales data for specific drugs are available from IQVIA and other claims data sources, why should the volume of sales be treated as confidential? Making it public would allow for independent assessment of the accuracy of reporting.

³ Both CBO and MedPac have standardized prescription sizes in Part D to 30 days’ supply in their published reports.

40.3 *Agreements on negotiation and renegotiation*: It is not clear the specific conditions under which a renegotiation will occur in subsequent years.

40.4 The negotiated drug should get favorable placement by the PBM/PDP. This will lower Medicare and Medicare beneficiary spending and give the drugs in the same therapeutic class the incentive to lower their prices. Medicare should prohibit spread pricing for these drugs.

Section 50: Negotiation Factors

50.1 The reporting of whether a pharmaceutical manufacturer recouped its costs should be subject to comparison with a CMS analysis of the individual components of data items related to R&D costs reported by the manufacturer and in SEC filings. This is because the assessment of whether costs were recouped is subject to a variety of arbitrary allocation and discounting assumptions that may not be applied by manufacturers in a fashion that is consistent with the public interest or best practices.

50.1 In considering prior federal financial support CMS might consider tax credits provided through the Orphan Drug program and similar subsidies in addition to grants and contracts that seem to be implied by this section.

50.2 Other countries conduct and compile comparative effectiveness studies. The negotiation process would benefit from review of the and the findings of these comparative effectiveness studies and the methods used by these countries. CMS should also examine the prices in these countries. The guidance should clarify whether studies conducted in other countries can be used in comparative effectiveness assessments.

50.2 CMS should specify how the comparative effectiveness of two drugs would be considered. If one drug is a cure and another drug requires ongoing treatment. For example, the price of a drug that is used to treat a chronic condition (arthritis) that is used continuously over years should be treated differently than the price of a drug that is used for a short period of time and then never again because a cure has been achieved (Hepatitis C drugs). The comparative effectiveness measure should examine the lifetime cost and effectiveness of both treatments.

50.2 The guidance notes that CMS will use FDA approved prescribing information in the negotiation process. The information that is contained on the product labels should guide CMS in defining a drug's use.

50.2 There are well-developed alternatives to QALYs that are not subject to concerns about disadvantaging older adults or disabled people, including "equal value life year gained" (evLYG). They have been employed in numerous settings for reasons precisely consistent with Congressional intent. In addition, metrics such as the Health Years in Total (HYT) and the Global Risk Adjusted QALY (GRA-QALY) address potential discriminatory features of QALYs and in some cases create a unique advantage for people with disabilities.

Section 60: Negotiation Process

60.1 *Establishment of a single price:* Some drugs are taken for a certain number of months while others are taken the full year. How will this be translated into 30-day equivalents. For example, if a drug needs to be taken for only four months during the year, how will that be translated into 30-day equivalents? In such cases, annual spending levels are appropriate.

60.1 The use of a single price is sensible and consistent with the definition of a drug set forth in Section 30.

60.1 In discussing the determination of a single price, the Guidance uses the term cost (second paragraph under 60.1). That is imprecise because the data being referred to may be either payments or prices and not costs.

60.3 Therapeutic class

- a. Some brand name drugs are the only option to treat a disease, while others have one or more brand name alternatives available. The PDPs have more negotiating power when there is one or more different brand name drugs that can address the same condition.
- b. The challenge is to define the therapeutic categories that define the competing brand name drugs. One commonly used product was developed by US Pharmacopeia, but there are others including the Veterans Affairs (VA) classification code, Medi-Span Generic Product Identifier (GPI), or the IQVIA Uniform System of Classification (USC) that has been used by the Centers for Disease Control and Prevention (CDC).
- c. Each of these efforts define a therapeutic category somewhat differently and these differences result in different combinations of drugs in the therapeutic category. Some of the factors explaining the differences include therapeutic category, pharmacology (mechanism of action), chemical structure, and indication.
- d. The Guidance should recognize that differing approaches across products are likely to best serve balancing market and clinical issues and having all the different ways to measure therapeutic alternatives available. CMS would be well served to commission a study of the different ways to measure therapeutic class and the strengths and weaknesses of the different existing products. This will help CMS respond to the statements by the drug companies that a drug has brand name competitors according to some measure.
- e. It is therefore likely that the best approach to analysis will be drug specific.

60.3 The Part D net price for the alternative therapeutic drugs should include the rebates. Additional data should be collected on the alternative therapeutic drug in addition to price. So that the true market context for establishing transaction prices is considered by CMS in its negotiating position.

60.3.2 It should be made clear that generic drugs will be included in the drugs that are considered therapeutic alternatives in making the initial price offer by CMS.

60.3.2 In adjusting starting prices using comparative effectiveness analysis, it is important to consider how the differences in effectiveness among alternatives would translate into price differentials. This will need to be done on a drug-by-drug basis depending on the circumstances of the negotiated drug and the other drugs in the therapeutic class.

60.3.3.1 The discussion of the effectiveness of therapeutic alternatives proposes to use health outcomes, patient experience, etc. This is appropriate. The Guidance should distinguish clearly how these differ from QALYs (see 50.2 above).

60.4.4 The process set out in this section is appropriate. The evidence on negotiation processes from collective bargaining and other structured negotiations shows that key ingredients are 1) holding informal meeting to discuss issues and identify key pressure points; 2) regular communication; and 3) transparency with respect to how each side is using information. The process outlined in this section might benefit from allowance for additional, less formal meetings or some other channel for communication. Also, establishing some further guidance in the future on how data will be used may further promote reaching agreements in the negotiations. This can be specified after the first round of negotiations.

An issue not discussed in the Guidance – it is unclear if indication-based pricing will be permitted. Indication pricing should be taken into account, but those prices should be combined into the one composite price.

Thank you for your attention to these comments.

Sincerely,

Gerard Anderson and Richard G. Frank

Appendix

1. Examples of studies offering evidence on this point include the following:

S. Dong-Churl, W.G. Manning Jr., S. Schondelmeyer, and R.S. Hadsall, “Effect of Multiple-Source Entry on Price Competition After Patent Expiration in the Pharmaceutical Industry,” *Health Services Research*, 35(2), June 2000, pp. 529-547;

Congressional Budget Office, *op. cit.*, pp. 28-29;

H. Grabowski and J. Vernon, “Brand Loyalty, Entry, and Price Competition in Pharmaceuticals after the 1984 Drug Act,” *Journal of Law and Economics*, 35(2), October 1992, pp. 331-350;

R.G. Frank and D.S. Salkever, “Generic Entry and the Pricing of Pharmaceuticals,” *Journal of Economics & Management Strategy*, 6(1), Spring 1997, pp. 75-90;

Caves, *et al.*, *op. cit.*;

D. Reiffen, and M.R. Ward, “Generic Drug Industry Dynamics,” *The Review of Economics and Statistics*, 87(1), February 2005, pp. 37-49;

A. Saha, H. Grabowski, H. Birnbaum, P. Greenberg, and O. Bizan, “Generic Competition in the US Pharmaceutical Industry,” *International Journal of the Economics of Business*, 13(1), February 2006, pp. 15-38;

H.G. Grabowski, *et al.*, “Updated Trends in US Brand-Name and Generic Drug Competition,” *Journal of Medical Economics*, 19(9), April 2016, pp. 836-844;

R.G. Frank and R.S. Hartman, “The Nature of Pharmaceutical Competition: Implications for Antitrust Analysis,” *International Journal of the Economics of Business*, 22(2), 2015, pp. 301-343;

R.G. Frank, T.G. McGuire, and I. Nason, The Evolution of Supply and Demand in Markets for Generic Drugs, *Milbank Quarterly* 99(3):828-852 September published online June 1, 2021

2. Ariel Dora Stern et al., Biosimilars And Follow-On Products In The United States: Adoption, Prices, And Users Health Affairs June 2021;

Frank RG, M Shahzad, WB Feldman, AS Kesselheim, Biosimilar Competition: Early Learning, *Health Economics* 12 January 2022 <https://doi.org/10.1002/hec.4471>;

Biosimilars in the United States 2023-2027 - IQVIA

Dr. Steven J Potts, Ph.D, MBA
Founding CEO
Anticipate Biosciences
April 11, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
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IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

As Founding CEO of Anticipate Biosciences I appreciate the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

2.3 million women annually worldwide are diagnosed with breast cancer - 80% are estrogen receptor positive. Despite remarkable improvements to treat these cancers over decades of drug development, many women will die from recurrence of their disease. The standard of care for recurrent or metastatic ER+ disease is endocrine therapy. However, these cancers eventually progress, often due to the acquired mutations of the estrogen receptor in the form of ESR1 mutations. A novel drug class, called ErSO, provides a unique mechanism of action by binding to the estrogen receptor and invoking cancer cell death in a manner that is independent of estrogen and is therefore not a form of endocrine therapy but instead utilizes a novel mechanism against the anticipatory stress pathway that is unique to ER+ cells, either ESR1mutant or not. The optimized molecule of this drug class, ErSO-02, is planned to enter clinical trials in 2024 and has the potential to transform therapy in breast cancer patients who no longer respond to existing treatments.

I have been fundraising for a Series A to support our clinical trials and since the passage of the IRA have noticed a distinct change in the appetite of investors for small molecule drug development. Curious as to what caused this change, I conducted a personal grassroots survey online of nearly 100 biotech investors and CEOs. What I found is deeply disturbing for the future of oncology drug development. Six of every seven investors have already moved away from funding small molecule drug development programs for the elderly and large populations because of the passage of IRA and the inability to sustain investment with the nine-year negotiation clock for small molecules and other NDA-path medicines. The results can be found here: <https://www.nopatientsleftbehind.org/publications/ira-impact-on-small-molecule-development>

I am aware that CMS is not soliciting comments on Section 30 but I am including the comments that would have been made had comments been permitted.

Comments: Section 30.1 Medicare negotiation for NDA-path drugs at nine-years post-launch

As mentioned above, six of every seven biotech investors that I surveyed are already moving away from funding small molecule drug development for the elderly or large populations as a result of the IRA. This is a disaster for small biotech companies such as Anticipate Bioscience. Nine years is not adequate time for investors to make back their investment. It's much shorter than the average 14-years of exclusivity typically afforded by patent protection. Furthermore, small molecule drug development is equally risky to biologicals, and of the programs that enter human clinical trials, in oncology less than 10% actually become approved drugs.

In both neurodegenerative diseases (Alzheimer's, Parkinson's, etc.) and cancer brain metastases, small molecules are the weapon of choice over biologics given their ability to penetrate the blood brain barrier. If I make a biologic and it kills off all cancer cells in the body but cannot cross the blood brain barrier, the cancer will come back with a vengeance with lethal brain metastases. We need both small molecules and biologics weapons in our toolkit. We need 13 years for small molecules, as we have for biologics, in order for investors to continue supporting this area.

Comments: Section 30.1.1: To be considered for the orphan drug exclusion, the drug or biological product must (1) be designated as a drug for only one rare disease or condition under section 526 of the FD&C Act and (2) be approved by the FDA only for one or more indications within such designated rare disease or condition.

The damage from IRA's treatment of orphan drugs could be mostly alleviated by creating small- and large-molecule parity for negotiation at 13 years (see Section 30.1 above).

In oncology we try to focus our development efforts initially on a small cancer area, where we will see the most likely and strongest benefit. For Anticipate Biosciences it is a genomically defined subset of ER+ metastatic breast cancer, which would be an orphan drug area based on overall numbers. However, after that we would seek to attack cancers for all ER+ breast cancer and likely also unmet needs in ovarian and endometrial cancers. However, the IRA disincentivizes us from expanding beyond this initial population because we would lose our Orphan Drug exemption to the negotiation process.

Comments: Section 50.2: CMS' processes for determining the Maximum Fair Price for individual medicines as well as the relevance of "therapeutic alternatives" to the drugs it selects for negotiation.

To the extent that CMS wants to appreciate the value that a medicine brings to society before it decides how aggressively to lower its price (particularly in the case of NDA-path drugs that experience negotiation far sooner than they would have gone generic), CMS should broadly account for a medicine's value elements, using a dynamic stacked cohort model that accounts for value to patients, to caregivers, and to the rest of the population whose risk is reduced by having the drug (i.e., if it's going to do CEA, do generalized CEA, not conventional over-simplified CEA).

CMS should consider key product attributes like efficacy, safety, and ease-of-use in determining relevant "therapeutic alternatives" (the basis for CMS' opening bid).

Comments: Section 40.2.2. CMS prohibitions on data disclosure and destruction of related documents.

I believe that CMS should be transparent in its processes for determining value and cost-effectiveness, versus the gag order and document destruction that are proposed today. It should be able to defend what it considers to be a "fair price," in the same way that I publicly have to defend my clinical trial data as part of the NDA approval process.

I am also concerned that this prohibition violates my company's First Amendment rights. I will need to be able to disclose to my board and investors what occurred in the negotiation process.

I appreciate your consideration of my comments as you develop Drug Price Negotiation Program policy. I look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact me by telephone at (858) 442-5896 or by e-mail at spotts23@anticipate.bio if you have any questions regarding our comments.

Best regards,



Steve Potts, Ph.D., MBA
Founding CEO
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Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Arcutis Biotherapeutics appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

By way of background, Arcutis is a small, publicly-traded (Nasdaq: ARQT) biotechnology firm focused on the development of innovative therapies for dermatological conditions. We currently have one FDA-approved product, and multiple other products currently in development.

- I. We oppose the discriminatory treatment afforded to small molecules compared to large molecules as established in the IRA and as outlined in Section 30.1, triggering Medicare negotiations for NDA-path drugs at nine years post-launch versus thirteen years post-launch for BLA-path drugs. The cost to develop a small molecule and a large molecule are roughly comparable, and the risk of failure for small molecules is if anything higher than for large molecules, so the financial risks are at least as great if not greater for small molecules, and there is no valid economic rationale for disadvantaging small molecule therapeutics. Rather, we believe that small and large molecules should be treated equally for the purposes of Medicare price negotiations.
- II. We do not agree with the CMS proposal that the orphan drug exclusion should only apply to therapies that are (1) designated as a drug for only one rare disease or condition under section 526 of the FD&C Act and (2) are approved by the FDA only for one or more indications within such designated rare disease or condition. CMS should look to only active orphan drug designations for the purposes of determining eligibility for the orphan drug exclusion (not including withdrawn orphan drug designations). Furthermore, the “bona fide marketing” standard is extra-statutory in nature with no basis in the law, which defines the standard simply as “marketed”. The proposed standard is ambiguous and subjective. The appropriate test, as specified in the IRA, is an objective, point-in-time determination of whether a drug has been “marketed,” which can be determined by reference to the “market date” reported by the manufacturer to the Medicaid Drug Rebate Program. It is defined as the date on which the

drug is first sold in the US, and is the standard that CMS is using to determine whether a drug is marketed for purposes of the MDRP, the Part D inflation rebate guidance, and ASP (where the standard is articulated slightly different as the "first sale date.")

- III. We are concerned by the provisions contained in Section 50.2 regarding Maximum Fair Price. The cost-effectiveness models employed by ICER exclude many demonstrable benefits of medicines, resulting in extreme under-estimations of the value of new medicines. CMS should broadly account for a medicine's value elements, using a dynamic stacked cohort model that accounts for value to patients, to caregivers, and to the rest of the population whose risk is reduced by having the drug. Additionally, we believe CMS should consider key product attributes like efficacy, safety, and ease-of-use in determining relevant "therapeutic alternatives" for "Maximum Fair Price" determinations.
- IV. We are also concerned by the provisions contained within section 90.4 regarding determination of generic or biosimilar competition. The proposed standard of "bona fide" competition is unnecessarily and insupportably vague, and could give rise to situations where innovator products are subject to both generic competition and CMS price negotiations. This provision could perversely reduce generic competition, ultimately leading to higher prices generic drugs across society.
- V. We are alarmed by the prohibitions on data disclosure contained in section 40.2.2. CMS's process for determining value and cost-effectiveness should be transparent, and CMS should publicly defend what it considers to be a "fair price." Furthermore, this prohibition violates the First Amendment rights of companies covered by the CMS negotiations. Companies subject to the negotiation process need to be able to disclose to their boards and their investors what occurred in the negotiation process.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact me by telephone at 805-418-5006 or by e-mail at tfw@arcutis.com. If you have any questions regarding our comments.

Sincerely,

Frank Watanabe
President and CEO



April 14, 2023

Via E-mail

Administrator Chiquita Brooks-LaSure
Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health & Human Services
7500 Security Boulevard
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure and Deputy Administrator Seshamani:

argenx US, Inc. ("argenx") thanks the Centers for Medicare and Medicaid Services ("CMS" or the "Agency") for the opportunity to submit comments on the Agency's Initial Memorandum on the Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026 (hereinafter, "Medicare Drug Price Negotiation Program Guidance" or "Guidance"), under Section 11001 of the Inflation Reduction Act ("IRA").¹

argenx is a global immunology company committed to improving the lives of people suffering from severe autoimmune diseases. argenx partners its antibody engineering capabilities with leading academic researchers to collaborate on breakthrough research and publications to create potential new treatment options. We have a robust pipeline that starts with strong science and is aimed at translating immunology breakthroughs into differentiated medicines. We engineer first-in-class therapies for rare diseases – where underserved patients need breakthrough therapies and the healthcare community needs viable options.

Our first approved product, VYVGART® (efgartigimod alfa-fcab) is indicated for the treatment of generalized myasthenia gravis ("gMG") in adult patients who are anti-acetylcholine receptor ("AChR") antibody positive, who represent 85% of the total gMG population. gMG is a rare and chronic neuromuscular disease characterized by debilitating and potentially life-threatening muscle weakness. VYVGART, designated as an orphan drug, is the first and only FDA-approved neonatal Fc receptor ("FcRn") blocker and the first approved therapy designed to reduce pathogenic IgGs. Our pipeline includes studies targeting diseases, including orphan diseases, in neurology, hematology, rheumatology, dermatology, and nephrology.

It is with this experience and on behalf of the Medicare patient populations we serve that argenx respectfully submits the following comments.

Executive Summary

As further detailed below argenx requests that CMS consider the following:

- work with Congress to expand the definition of orphan drugs to include drugs that may be designated as a drug for one *or more* rare diseases or conditions, rather than drugs that are designated for *only one* rare disease or condition.
- clarify that obtaining additional indications for a small molecule or biologic within the same orphan disease will not exclude the drug from the orphan designation exception.

¹ See Medicare Drug Price Negotiation Program Guidance, available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

- if a question arises regarding whether a drug or biological is a fixed combination drug, argenx urges CMS to look to the FDA regulatory communications and databases to identify active ingredients or moieties.
- provide updated guidance clarifying that new formulations refers only to drugs approved under the *same* NDA or BLA, and not drugs approved under separate NDAs or BLAs.

I. Orphan Drugs

The Orphan Drug Act (“ODA”) was enacted by Congress to help spur investment and discovery in the rare disease space. The incentives provided by the ODA have enabled companies to bring innovative and lifesaving treatments to the rare disease community. However, this successful multi-decade policy needs continuous support to further the vital research and contribution to vulnerable patient populations. Under the IRA, orphan drugs are not qualifying single source drugs.² The statute defines an orphan drug, in this section, as “[a] drug that is designated as a drug for only one rare disease or condition under section 526 of the Federal Food, Drug, and Cosmetic Act and for which the only approved indication (or indications) is for such disease or condition.” As CMS states in the Guidance, orphan drugs are excluded from the IRA’s Medicare Drug Negotiation Program if the drug or biological product is (1) designated as a drug for only one rare disease or condition under section 526 of the Food, Drug & Cosmetic Act and (2) approved by the FDA only for one or more indications within such designated rare disease or condition.³

At argenx, we innovate by developing drugs against fully novel target biology with the aim to open up new routes of treatment for patients; including indications that previously have been underserved. Through this approach, our compounds are typically able and have been specifically designed to address unmet need in multiple orphan indications. For example, we continue to study efgartigimod alfa-fcab (which has been approved by the FDA and received orphan designation for its first indication gMG) in multiple other indications including other rare diseases. We are concerned that the one orphan disease designation requirement of the orphan designation exemption may unintentionally stifle innovation by creating a tradeoff of unmet need of one patient group over another, instead of fostering benefit for the broadest possible patient population.

argenx appreciates CMS’s understanding of the value of orphan drug development and the Agency’s consideration to take additional actions to “best support orphan drug development.”⁴ Accordingly, argenx strongly encourages CMS to:

- work with Congress to expand the definition of orphan drugs to include drugs that may be designated as a drug for one *or more* rare diseases or conditions, rather than drugs that are designated for *only one* rare disease or condition; and
- clarify that obtaining additional indications for a small molecule or biologic within the same orphan disease will not exclude the drug from the orphan designation exception.

In addition to the above, we refer CMS to the comment submitted by Rare Disease Company Coalition (“RDCC”) on April 14, 2023. We fully support the recommendations made by RDCC regarding how CMS can mitigate the impact of the IRA’s orphan drug exclusion.

II. New Formulations

We are concerned that CMS’s approach of “us[ing] data aggregated across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended release formulation, and not based on the specific formulation, package size, or package type” would extend to products approved under different NDAs or BLAs.⁵ This position is in direct conflict with the plain language of the statute. CMS therefore has no authority to adopt or implement it.

² *Id.* at § 1192(e)(3).

³ Guidance at 10.

⁴ *Id.* at 11.

⁵ *Id.* at 7-8.

The statutory language clearly identifies and defines “qualifying single source drugs” as drugs approved under a new NDA or BLA.⁶ Further, a negotiation-eligible drug is a “qualifying single source drug” that is determined to be a high-spend drug under Part D or Part B, meaning the qualifying single source drug is among the 50 drugs with “the highest total expenditures” under Part D or Part B.⁷ Finally, a selected drug must be among the “negotiation-eligible drugs.”⁸ Accordingly, a selected drug *must* be a “qualifying single source drug,” which is a drug approved under a BLA or NDA. The new formulation language does not permit CMS to ignore the plain language of the statute that identifies each drug approved under an NDA or BLA as a separate qualifying single source drug. We urge CMS to issue updated guidance clarifying that new formulations refers only to drugs approved under the *same* NDA or BLA, and not drugs approved under separate NDAs or BLAs.

III. Fixed Combination Drugs

argenx supports the Guidance’s conclusion that fixed combination drugs with two or more active moieties / active ingredients should be considered as distinct products from a product containing only one (but not both) of the active moieties / active ingredients that is offered by the same NDA/BLA holder for the purpose of identifying qualifying single-source drugs.⁹ In other words, argenx agrees with the Guidance position that such combination products will not be aggregated with the formulations of the individual active ingredients of the fixed combination drug and will be considered a separate potential qualifying single source drug from the component moieties. CMS references FDA regulations to define “fixed combination drugs.” We further request that CMS codify this guidance into regulation.

We agree with CMS’s reliance on FDA to define what is meant by a fixed combination drug. We further understand that CMS will rely on FDA’s determination of active ingredients or moieties, as included in a drug’s communications with FDA and the applicable databases.¹⁰ FDA has the appropriate experience and expertise to identify what components of a drug or biologic are considered an active ingredient or moiety and CMS should defer to such experience and expertise. If a question arises regarding whether a drug or biological is a fixed combination drug, argenx urges CMS to look to the FDA regulatory communications and databases to identify active ingredients or moieties.

⁶ Inflation Reduction Act of 2022, Pub. L. No. 117-169, SSA § 1192(e)(1)(A)-(B) (defined as “A drug—(i) that is approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act and is marketed pursuant to such approval” or “[a] biological product—“(i) that is licensed under section 351(a) of the Public Health Service Act and is marketed under section 351 of such Act”).


⁷ *Id.* at § 1192(d)(1).

⁸ *Id.* at § 1192(b).

⁹ Guidance at 9.

¹⁰ See e.g., FDA, Drugs@FDA listing “Active Ingredients,” available at <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm>.

At argenx we are working every day to put forward new innovations in drug therapies that will transform the lives of patients living with rare and debilitating disease. We recognize the important part that policymakers play in market access and how our therapies can get to the patients that need it most. We appreciate this opportunity to comment on the Guidance. If you have any questions about these comments, please do not hesitate to contact me at wrichards@argenx.com.

DocuSigned by:
Sincerely,

D63808F86C5E4DB...

William Richards
Head US Market Access



Arizona Bioindustry Association, Inc.
1800 E Ray Road, Suite A-106
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The Honorable Chiquita Brooks-LaSure
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April 14, 2023

VIA ELECTRONIC DELIVERY

IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Brooks-LaSure,

Thank you for the opportunity to offer public comment on the initial guidance regarding the Drug Price Negotiation Program under the Inflation Reduction Act of 2022 (IRA) issued by the Centers for Medicare & Medicaid Services (CMS) on March 15, 2023.

My name is Joan Koerber-Walker. I have the privilege to serve as the President & CEO of the Arizona Bioindustry Association (AZBio). Our community represents Arizona's health innovation sector including patient groups, biotech and medtech companies of all sizes, Arizona's universities and community colleges, research institutes, and healthcare institutions. AZBio member organizations employ over 300,000 Arizonans.

On a personal note, my training and education is in economics. During a career spanning over four decades, I have had the opportunity to work in both the for profit and nonprofit sectors. My career experience includes executive leadership, distribution and value chains, organizational systems design, and economic modeling. Today, I am 62 years of age. In just a few short years, I will be a Medicare Beneficiary.

The Inflation Reduction Act (IRA) of 2022 (P.L. 117-169) includes significant and much needed improvements to Medicare coverage that will provide our senior citizens with more opportunity to access the medicines they need. Capping the out-of-pocket cost of insulin to \$35 will make life better for a growing number of seniors who depend on this life saving medicine. Establishing a yearly cap (\$2,000 in 2025) on out-of-pocket prescription drug costs in Medicare will be a welcome relief to seniors who rely on medicines to maintain their health or manage disease. For some, even this amount will be too high, but it is an improvement. Expansion of the low-income subsidy program (LIS or "Extra Help") under Medicare Part D to 150% of the federal poverty level starting in 2024 will address affordability for more seniors. Finally, providing access to recommended adult vaccines without cost-sharing will hopefully encourage more of our seniors to proactively protect their health by avoiding the burden of preventable

diseases. In addition to the patient benefit, these improvements should have a positive impact on our nation's growing levels of Cost-related Non-adherence (CRN).

Improved medical adherence lowers overall health care costs. When people are able to better manage their health and health conditions, they can avoid CRN related complications. A 2018 studyⁱ reported increased costs related to poor adherence to medications for common chronic conditions like diabetes, heart failure, high cholesterol, and hypertension resulted in an estimated annual cost of drug-related morbidity and mortality resulting from nonoptimized medication therapy was \$528.4 billion, equivalent to 16% of total US health care expenditures in 2016.

Reducing the rising costs of healthcare is essential. By 2030, all Baby Boomers will be age 65 or older. At that time, the 65 and older population is projected to be over 71 million. The 75 and older population is projected to be over 33 million.ⁱⁱ Providing quality health services to this population is Medicare's charter and responsibility. A goal of the IRA is to manage/lower the cost of doing so.

The previously discussed provisions to improve a patient's ability to afford their medicines and lower overall rates of CRN will support this goal.

Other provisions of the IRA create challenges that may undermine achieving this the goal. Due to advancements in medical science, we are living longer and living better. Yet, with all of our progress, we still lack the ability to prevent, cure, or even effectively treat some of our greatest health challenges. Health innovations related to significant Medicare cost drivers must be priority. These include, but are not limited to, heart disease and stroke, cancer, diabetes, arthritis, and Alzheimer's disease.

Medicare Drug Price Negotiation

Your summary states: "Medicare will be able to negotiate directly with drug manufacturers to lower the price of some of the costliest single-source brand-name Medicare Part B and Part D drugs. This means that people with Medicare will have increased access to innovative, life-saving treatments, and the costs will be lower for both them and Medicare"ⁱⁱⁱ

In the short term, Medicare's ability to negotiate directly with drug manufacturers to lower the price of some of the costliest single-source brand-name Medicare Part B and Part D drugs will reduce costs, but it is also already beginning to create adverse effects in the health innovation ecosystem.

These adverse effects are changing the risk/reward calculation that investors use to make decisions on which small health innovation companies they will invest in. When the risks are high, as they are in drug development, and the rewards decline, so will investment. Investors have many options beyond health innovation. If the investment dollars shift to other innovation sectors, people with Medicare will have reduced access to innovative, life-saving treatments, and the costs for Medicare will continue to increase due to the projected demographics.

Congress created the IRA. CMS through its rule making will implement it. The Biotechnology Innovation Organization (BIO) has separately submitted extensive comments on its concerns and points of consideration relative to implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026. Having reviewed these comments, we are in full agreement. These recommendations will support implementation without expanding on the Congressional intent.

Since the IRA was signed in August of 2022, AZBio has consulted with our patient groups, health innovators, and the investment community. A major theme originating from these discussions was the essential need to not slow the progress of future treatments and cures. These create hope for Medicare Beneficiaries and our best opportunity to reduce the overall cost of healthcare in the long term. The rules you finalize can minimize potential disruption of the innovation process or aggravate it. We sincerely hope that you will give serious consideration to BIO's comments.

The following example demonstrates why this is so important. It uses one Arizona health innovation that is under development to address one of Medicare's major health challenges. Similar examples are available for other conditions.

The Health Challenge: Alzheimer's Disease

According to the Alzheimer's Association, "with the aging of the baby boomers, the number of Americans aged 65 and older with Alzheimer's is expected to dramatically escalate."^{iv}

- Today, an estimated 5.8 million Americans aged 65 and older are living with Alzheimer's disease.
- By 2050, there are projected to be nearly a million new cases every year, with another American developing Alzheimer's every 33 seconds.
- The number of Americans living with Alzheimer's will nearly triple by 2050 to 13.8 million if nothing changes.
- Costs will also expand in lockstep. By 2050, combined Medicare and Medicaid spending on people with Alzheimer's will skyrocket to \$777 billion (in 2020 dollars)
- In 2050, Medicare spending on people with Alzheimer's will total \$584 billion—an increase of 278% from today's spending levels. This will represent more than 1 in every 3 dollars of total estimated Medicare spending.
- Medicaid spending on people with Alzheimer's will increase 278% between now and 2050, as costs will reach \$194 billion in 2050.

Developing Health Innovation

Currently an Arizona small business (Company) has a vision to prevent, halt and cure neurodegenerative diseases. The Company has begun clinical trials on a regenerative treatment for Alzheimer's Disease and other neurodegenerative diseases. They believe this health innovation has the potential to not only halt but to reverse the disease's progression. It is currently undergoing a Phase 2b study in patients with mild Alzheimer's Disease. Significant support from both government and philanthropic partners helped the company to progress to its current stage. To undertake the final studies, private investment will be essential. Drug development for Alzheimer's disease has a long history of highly publicized and expensive clinical failures. Attracting private investment for even the most promising drug candidates is a challenge. Due to the significant size of the patient population, the clinical trials will need to be extremely large to prove statistical significance. This makes the regulatory timeline longer and drives the cost much higher than other investment options an investor may be considering. These are significant risk factors in the risk/reward calculation.

The IRA has raised new challenges:

- The company's drug candidate is classified as a small molecule. As such it will only be exempt from negotiation for 9 years from its FDA-approval or licensure date as compared with the 13-year exemption available for biological products.
- If the Company's health innovation achieves its clinical milestones and receives FDA approval, its products will be in high demand. It is likely that it will be on the list for price negotiation as soon as it is eligible. This effectively reduces the investors perceived reward. With a such a "high risk"

investment, any reduction on the reward side of the equation makes fundraising more of a challenge and takes longer to accomplish.

- Longer fundraising cycles delay the clinical trial process while patients continue to suffer, and costs continue to climb.

This is just one Arizona example. Today, our health innovators are working to deliver better treatment options for patients with cancer, diabetes, cardiovascular and pulmonary diseases, autoimmune diseases, and neurological diseases.

Summary

In conclusion, the IRA contains provisions that reduce patient out-of-pocket costs, relieve some of the financial burdens patients face, and hopefully will reduce costs through lowering CRN levels. This alone will not be enough to bend the healthcare cost curve that is being driven ever higher due to our aging population demographic.

While price negotiation will provide some relief, even this will not be enough to bend the cost curve enough to balance the increasing costs of acute and chronic disease for a growing Medicare population.

Health innovation, in the form of new treatments that can prevent, treat, and cure, is our best cost containment strategy and presents new hope for patients.

CMS, through the rule making process, can help to minimize the disruption that the IRA is creating in the health innovation ecosystem by giving careful consideration to the recommendations provided by BIO and other members of the health innovation community.

Thank you for taking the time to review my comments. I appreciate this opportunity to provide feedback to CMS on the Initial Guidance. Should you have any questions, please do not hesitate to contact me at jkw@azbio.org or at (480)332-9636.

Sincerely,



Joan Koerber-Walker
President & CEO

Arizona Bioindustry Association, Inc.

ⁱ Watanabe JH, McInnis T, Hirsch JD. Cost of prescription drug related morbidity and mortality. Ann Pharmacother. 2018 Sep;52(9):829-837.

ⁱⁱ Centers for Disease Control and Prevention, National Center for Health Statistics. Health, United States, 2005: With chartbook on trends in the health of Americans. Atlanta, GA: Centers for Disease Control and Prevention; 2005. [http://www.cdc.gov/nchs/data/05.pdf](http://www.cdc.gov/nchs/data/hus/05.pdf)

ⁱⁱⁱ <https://www.cms.gov/inflation-reduction-act-and-medicare>

^{iv} https://act.alz.org/site/DocServer/2012_Costs_Fact_Sheet_version_2.pdf?docID=7161



April 14, 2023

Chiquita Brooks-LaSure, Administrator
Centers for Medicare and Medicaid Services
Hubert H. Humphrey Building
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Administrator Brooks-LaSure:

Arnold Ventures welcomes the opportunity to provide comments to the Centers for Medicare and Medicaid Services (CMS) on the following guidance issued on March 15, 2023:

- *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments*

Arnold Ventures is a philanthropy dedicated to investing in evidence-based policy solutions that maximize opportunity and minimize injustice. Our work within the health care sector is driven by the recognition that the system costs too much and fails to adequately care for the people it serves. Our work spans a range of issues including commercial-sector prices, provider payment incentives, prescription drug prices, clinical trials, Medicare sustainability, and complex care.

We thank you for the opportunity to provide comments on the Medicare negotiation process. This letter is organized into 6 sections as follows:

1. Preventing Product Line Extensions from Undermining the Negotiation Framework, which includes comments on the following:
 - *Section 30 - Identification of Selected Drugs for Initial Price Applicability Year 2026*
 - *Section 60.5.1 Application of the MFP to New NDAs/BLAs or NDCs*
 - *Section 90.4 - Monitoring for Bona Fide Marketing of Generic or Biosimilar Product*
 - *Section 120 - Application of Medicare Part B and Part D Prescription Drug Inflation Rebate Programs to Selected Drugs*
2. Bringing Market Competition into the Negotiation Process, which includes comments on the following:
 - *Section 60.3.2 - Developing a Starting Point for the Initial Offer*
 - *Section 60.3.4 - Considerations of Manufacturer-Specific Data*
3. Assessing Research and Development Costs and Returns, which includes comments on the calculation of total research and development costs for selected drugs outlined in Appendix C.
4. Balancing Needs for Confidentiality with Public Interest in Transparency, which includes comments on the following:
 - *Section 60.6.1 - Explanation for the MFP*
5. Delay in Negotiations for Certain Biologics with High Likelihood of Biosimilar Entry, which include comments on the following:
 - *Sections 30.3.1.1 to 30.3.1.4 Delay in the Selection and Negotiation of Certain Biologics with High Likelihood of Biosimilar Entry*



6. Other Provisions in the Guidance that help to Strengthen the Negotiation Framework, which include comments on the following:
- Section 50.2 - Evidence About Therapeutic Alternatives for the Selected Drug
 - Section 60.3.3.1 - Analysis for Selected Drugs with Therapeutic Alternative(s)
 - Section 60.4 Negotiation Process
 - Section 60.5 Application of the MFP Across Dosage Forms and Strengths
 - Section 80 – MFP Eligible Individuals

We want to thank you and CMS staff for your important and expeditious work implementing the prescription drug provisions of the Inflation Reduction Act (IRA) and for the opportunity to provide input. We recognize the difficulty of the task you face.

Section 1. Preventing Product Line Extensions from Undermining the Negotiation Framework

Section 30 - Identification of Selected Drugs for Initial Price Applicability Year 2026

Arnold Ventures strongly supports the process for selecting drugs for negotiation outlined in Section 30. Importantly, the guidance includes the following provisions that are critical to blocking new formulations of selected drugs from delaying negotiations indefinitely by shifting utilization toward modified versions:

- Defining a qualifying single source drug as all dosage forms and strengths of the drug with the same active moiety (or active ingredient in the case of biologics) marketed by the same manufacturer.
- Determining the time that the qualifying single source drug has been on the market using the earliest date of approval or licensure for the active moiety/active ingredient across all NDA and BLA applications.

Section 60.5.1 Application of the MFP to New NDAs/BLAs or NDCs

CMS is seeking comment on the methodology to set Maximum Fair Prices (MFP) for new dosage forms of selected drugs that already have an MFP. Arnold Ventures recommends that CMS establish a methodology that ensures that the weighted average MFP across all dosage forms and strengths—including the new dosage form or strength of a selected drug—does not change from what it would have been had the new dosage form/strength not been introduced. This will prevent product line extensions from increasing the average MFP paid for the selected drug. This policy would also encourage manufacturers to introduce improved versions of their products earlier in the product's life cycle.

Section 90.4 - Monitoring for Bona Fide Marketing of Generic or Biosimilar Product

It is critical that CMS ensure that a competitive market is present to maximize savings from negotiation for patients and taxpayers. Arnold Ventures strongly recommends that generic market share be assessed at the active moiety/active ingredient level when determining when to lift the MFP from a selected drug with meaningful generic or biosimilar competition.



The Secretary could apply a threshold generic market share at the active moiety/active ingredient level that is consistent with the literature on competitive generic markets.¹ This would be at least half of the market for small molecule drugs and at least quarter of the market for biosimilars.

Prescriptions could be standardized (such as a 30-day supply in Part D) to accurately estimate the market share of the generic product relative to the total volume dispensed to Medicare beneficiaries for the active moiety/active ingredient. The formula that determines generic market share would be calculated as the number of standardized prescriptions dispensed for the generic product divided by the number of standardized prescriptions dispensed for the selected drug aggregated across all dosage forms and strengths, plus the number of standardized prescriptions dispensed for the generic product.

Section 120 - Application of Medicare Part B and Part D Prescription Drug Inflation Rebate Programs to Selected Drugs

When CMS lifts the MFP from a selected drug with meaningful generic or biosimilar competition, the IRA requires that the base period used to calculate the drug's inflation penalty be reset. It is unclear how the MFP factors into the inflation rebate formula once the base period is reset, particularly whether it will be factored into the reset for Part D drugs.

Arnold Ventures recommends that manufacturer sales at the MFP be factored into the benchmark prices used to calculate inflation rebates in both Part B and Part D after the reset occurs for drugs that are no longer selected drugs. That would allow the reset to put downward pressure on prices consistently for previously selected Part B and Part D drugs. Otherwise, it is possible that the reset would put downward pressure on net prices in Part B but allow net prices in Part D to increase.

CMS is seeking comment on whether guidance should be issued for the inflation rebates in the Part B program for selected drugs before 2028. Arnold Ventures thinks it is important for CMS to issue additional guidance to ensure that stakeholders understand how MFPs will be factored into the inflation rebate calculations for selected drugs under both the Part D and Part B programs within the next year.

In sum, this section outlines Arnold Ventures' concerns about the amount that Medicare will pay for drugs after the MFP is lifted. If CMS were to choose a weaker definition of "robust and meaningful generic competition" then it would be even more important to implement the inflation rebate reset in a manner that is consistent with the intent of the IRA: that the reset of the inflation

¹ H.G. Grabowski, et al., "Updated Trends in US Brand-Name and Generic Drug Competition," *Journal of Medical Economics*, 19(9), April 2016, pp. 836-844; and R.G. Frank and R.S. Hartman, "The Nature of Pharmaceutical Competition: Implications for Antitrust Analysis," *International Journal of the Economics of Business*, 22(2), 2015, p.p. 301-343; R.G. Frank, T.G. McGuire, and I. Nason, "The Evolution of Supply and Demand in Markets for Generic Drugs," *Milbank Quarterly* 99(3):828-852 September published on-line June 1, 2021; Ariel Dora Stern et al. "Biosimilars And Follow-On Products In The United States: Adoption, Prices, And Users Health Affairs June 2021; and Frank RG, M Shahzad, WB Feldman, AS Kesselheim, "Biosimilar Competition: Early Learning," *Health Economics* 12 January 2022 <https://doi.org/10.1002/hec.4471>



rebate for previously selected drugs put downward pressure on the net prices paid for drugs by Medicare.

Section 2. Bringing Market Competition into the Negotiation Process

Section 60.3.2 - Developing a Starting Point for the Initial Offer

CMS proposed a methodology to develop a starting point price that could enable the Secretary to negotiate an MFP that is below the ceiling price. Arnold Ventures recommends that within the group of therapeutic alternatives used to establish the starting point price for the initial offer, that (1) those with higher-than-average net prices that do not offer any additional clinical benefits be dropped from the group before calculating a weighted average starting point price, and (2) generic and biosimilar therapeutic alternatives be included in the calculation.

Using the net prices in Part D (which include manufacturer rebates) is a helpful first step in bringing market competition into the negotiation process, but how CMS defines the group of therapeutic alternatives used to determine that starting point price is critical. For example, the Secretary should give greater weight in his initial offer to generics or biosimilars in the therapeutic group that are as effective as the selected drug.

When a selected drug has no therapeutic alternatives, CMS proposes to use Federal Supply Schedule (FSS) or Big 4 prices as the starting point price. These prices are tied to the lowest prices paid in the commercial sector. An issue with using recent FSS/Big 4 prices as the starting point price is that this will put upward pressure on those prices if the amount that Medicare pays is tied to them in some way.² An alternative domestic price reference for drugs with no therapeutic alternatives is the inflation adjusted FSS price or BIG4 price at launch.

Section 60.3.4 Considerations of Manufacturer Specific Data

As discussed in the guidance, Arnold Ventures supports lowering the initial offer if the manufacturer has recouped research and development costs, if federal funding supported the discovery or development of the drug, if there are multiple unexpired patents that will continue to protect the drug from generic or biosimilar competition for a number of years, or if the initial offer would otherwise exceed the average net price to the commercial sector.

Section 3. Assessing Research and Development Costs and Returns

CMS will include a portion of spending on “abandoned and failed” projects related to the same therapeutic area as the selected drug in its calculation of total research and development costs for the selected drug (Appendix C). While CMS should work to protect incentives for manufacturers to innovate, it also needs to ensure its policy is one that does not undermine the incentive to continue improving the efficiency of the research and development (R&D) process.

² For example, when Medicaid net prices were tied to FSS prices through the best price provision, FSS prices increased ([HRD-91-139 Medicaid: Changes in Drug Prices Paid by VA and DOD Since Enactment of Rebate Provisions \(gao.gov\)](#)). And this policy could also have similar effects to Medicaid’s best price provision which increased the prices paid by commercial payers ([1996doc20.pdf \(cbo.gov\)](#)).



CMS should clarify how large that portion is of total R&D costs and how far back in time the brand manufacturer may reach when considering “abandoned and failed projects.” Arnold Ventures recommends the following for CMS’s calculation of R&D costs and returns for selected drugs:

- Include spending on basic research for failed projects that occurred no more than 5 years before the basic research began.
- Post investigational new drug investments in abandoned and failed projects should be considered only if they occurred no more than 5 years before these types of investments began for the selected drug.
- Do not include spending on “abandoned and failed” projects that occurred after the selected drug was approved in the calculation of development costs.

If CMS were to choose to include investments in failed projects outside these timeframes, Arnold Ventures recommends that CMS adjust downward the portion of such costs that are counted toward R&D spending. That is because spending that occurred on failed projects long before the development of the selected drug began is less likely to be directly related to the development of the selected drug.

The portion of such spending that CMS chooses to allocate toward R&D costs could vary depending on how broadly the manufacturer reports these costs. The definition may be challenging to apply consistently across drugs and across manufacturers. Arnold Ventures recommends adjusting that portion depending upon how broadly the manufacturer has defined these types of costs (a broader definition would imply a lower portion).

The guidance states that spending on post-marketing clinical trials that were never completed will be included in R&D costs (Appendix C). Arnold Ventures does not believe that such costs should be included in estimated R&D costs if the deadline for completing those studies has passed. For example, manufacturers frequently do not complete post-marketing studies for drugs that receive accelerated approval in a timely manner. This behavior should not be rewarded by including the costs of post-marketing studies where the results are long overdue and incomplete as part of drug development costs considered under the negotiations framework. Arnold Ventures also recommends that only post-marketing studies that support Food and Drug Administration (FDA) approvals for new indications or new dosage forms be included in reported R&D costs.

CMS will need to collect data on R&D costs and returns on an annual basis to estimate the capitalized costs of R&D and the present discounted value of returns. Arnold Ventures also recommends including the cost of clinical trials in R&D costs only if those trials have been included in the clinicaltrials.gov database.

Section 4. Balancing Needs for Confidentiality with Public Interest in Transparency

Section 60.6.1 Explanation for the MFP

To support the integrity of the negotiation process, CMS needs to report to the public clearly the factors used to determine the MFP, which can be either at or below the statutory ceiling price. However, we recognize the challenge in doing so while preserving the confidentiality of the information manufacturers submit to CMS and of the negotiation process itself. Arnold Ventures recommends that CMS publish the following:



- Therapeutic alternatives used to formulate the starting point price/
- Relevant comparative effectiveness studies that adjusted the starting point price upward or downward.
- Directionally whether the Secretary was able to negotiate below the ceiling price.
- How much returns to R&D exceeded costs of R&D

CMS could publish a summary report covering all negotiated drugs in a cohort. This would enable CMS to provide more information to the public while protecting the confidentiality of data at the individual drug level. For example, CMS may be able to discuss in aggregate the following:

- How often the MFP is below the ceiling price.
- The MFP's average percentage reduction off the ceiling price.
- How much returns to R&D exceeded the costs of R&D.

The greater the transparency, the more confidence the public and key stakeholders will have in the negotiation process.

Additionally, CMS could acquire SSR Health and IQVIA data to estimate returns from marketing the drug. CMS could publish the present discounted value of the returns to marketing at the individual drug level based on these data (whereas using data submitted by manufacturers could have confidentiality issues). This would both be informative for the public and help CMS to verify the sales data submitted by the manufacturer.

Section 5. Delay in Negotiations for Certain Biologics with High Likelihood of Biosimilar Entry

Sections 30.3.1.1 to 30.3.1.4 Delay in the Selection and Negotiation of Certain Biologics with High Likelihood of Biosimilar Entry

Arnold Ventures supports the guidance on the implementation of the delay of negotiations related to biosimilar entry. Importantly, the provisions proposed by CMS in the guidance apply to the first cohort of selected drugs in 2023. These provisions make it more likely that 10 brand-name drugs will have an MFP in 2026 because fewer drugs will have dropped out during the negotiation process following biosimilar entry.

Arnold Ventures strongly recommends that CMS request additional information from the biosimilar manufacturer beyond what is listed in the guidance. It is imperative that CMS have the best available information to determine whether biosimilar entry is likely, and negotiations be delayed.

According to the guidance, CMS will determine that biosimilar entry is likely (and negotiations will be delayed) if there is a settlement agreement in place permitting biosimilar entry before September 1, 2025. CMS will not grant a delay in negotiations if there is ongoing patent litigation. The IRA and the guidance state that CMS will rely on settlement agreements submitted to the Federal Trade Commission (FTC) related to patent litigation as well as information submitted to the Securities and Exchange Commission (SEC) regarding business plans to make determinations regarding the likelihood of biosimilar entry.

The IRA gives the Secretary the ability to request additional information from the biosimilar manufacturer to help make this determination, but the guidance does not specify any additional information that CMS plans to request from the biosimilar manufacturer beyond that reported to the FTC, the FDA, and the SEC. For CMS to accurately assess when a biosimilar will enter the



market, Arnold Ventures strongly recommends that CMS use its authority under the IRA [1992(f)(1)(B)(ii)] to request the following additional information from the biosimilar manufacturer:

1. Whether it is part of ongoing litigation with respect to a patent covering the reference product.
2. All settlement agreements with the brand-name manufacturer of the reference biologic or other biosimilar manufacturers—whether they have been reported to the FTC or not.
 - This will help CMS to determine whether a settlement agreement has been reached that allows biosimilar entry to occur within the window and whether there are any agreements in place with anti-competitive provisions. The terms of any “covenant not to sue” received from the brand manufacturer with respect to any unexpired patent should also be reported to CMS.
3. If there is no ongoing litigation reported, and if no settlement agreement exists specifying a date of entry during the window, the biosimilar manufacturer should identify any unexpired patents that are preventing its entry and when those patents will expire.
4. If the biosimilar manufacturer officially exchanged patent information with the brand manufacturer after filing its application with the FDA (that is, engaged in a “patent dance”), the results of that information exchange should be shared with CMS.³

Finally, Arnold Ventures recommends that if a delay request has been submitted by a biosimilar manufacturer, that CMS obtain from the FTC all settlement agreements that are related to the reference biologic (including those that involve other biosimilar manufacturers) to help determine whether biosimilar entry is likely.

Section 6. Other Provisions in the Guidance That Help to Strengthen the Negotiation Framework

Arnold Ventures supports CMS’s guidance outlined in the following sections:

1. *Section 40 – Entering into Agreements with Manufacturers of Selected Drugs.*
2. *Section 50.2 - Evidence About Therapeutic Alternatives for the Selected Drug.* We support CMS’s consideration of evidence on therapeutic substitutes, clinical effectiveness, and cost effectiveness that values all lives equally submitted from all public sources including academics and clinicians.
3. *Section 60.3.3.1 - Analysis for Selected Drugs with Therapeutic Alternative(s),* which outlines the qualitative approach to use information on comparative effectiveness to adjust the starting point price.
4. *Section 60.4 Negotiation Process,* which includes process steps (initial offer from CMS, response from manufacturer followed by up to 3 meetings), final written offer by CMS, and then acceptance or rejection by manufacturer.
5. *Section 60.5 Application of the MFP Across Dosage Forms and Strengths,* which specifies the methodology to apply MFPs across dosage forms and strengths for drugs selected for negotiation in 2023. In future years, CMS could consider using Average Manufacturer Prices (AMPs) (actual transaction prices that are close to list prices and reported to CMS under the Medicaid rebate program) in the formula to apply the MFP across dosage forms and strengths rather than Wholesale Acquisition Cost (WAC) prices. While it is unclear

³ Robin Feldman, *Purple Is the New Orange* (forthcoming ILLINOIS L. REV.)



whether manufacturers would engage in this practice, current and future WAC prices can be more easily manipulated by the manufacturer than the AMPs.

6. *Section 80 – MFP Eligible Individuals*, which clarifies that the MFP applies to physician administered drugs taken by beneficiaries in Medicare Advantage Plans

Conclusion

Arnold Ventures is prepared to assist with any additional information needed. Comments were prepared by Anna Anderson-Cook, Ph.D. with assistance from Andrea Noda, MPP, Vice President of Health Care at Arnold Ventures and Mark E. Miller, Ph.D., Executive Vice President of Health Care at Arnold Ventures.

Please contact Andrea Noda at anoda@arnoldventures.org or Mark E. Miller, Ph.D. at mmiller@arnoldventures.org with any questions. Thank you again for the opportunity to comment and for your important work to lower prescription drug prices for the Medicare program and its beneficiaries.

Sincerely,

Andrea Noda



April 14, 2023

Dr. Meena Seshamani, M.D., Ph.D
Deputy Administrator and Director of the Center for Medicare
U.S. Department of Health and Human Services
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244

Submitted via IRAREbateandNegotiation@cms.hhs.gov

RE: Solicitation of Comments; Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Deputy Administrator Seshamani,

The Association for Accessible Medicines (AAM) and its Biosimilars Council appreciates the opportunity to provide comments in response to the *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments*.

AAM is the nation's leading trade association for manufacturers of generic and biosimilar prescription medicines. AAM's core mission is to improve the lives of patients by advancing timely access to affordable, FDA-approved generic and biosimilar medicines. The Biosimilars Council works to increase patient access to lifesaving, high-value biosimilar medicines. Over the last ten years, generic and biosimilar medicines have provided more than \$2.6 trillion in savings to U.S. patients and the healthcare system. In 2021 alone, these medicines provided more than \$373 billion in savings, including more than \$119 billion in savings for the Medicare program.¹ Because of their low cost and high value, generic and biosimilar medicines today account for more than 91% of all prescriptions dispensed in the US but only 18% of drug spending.

We are concerned by several key aspects of the approach outlined in the Initial Memorandum. These concerns, and suggested alternative approaches, are described below:

CMS Should Determine Marketing Status of Generic Drugs or Biosimilar Biological Products Based on Marketing, Not Sales [Section 30 – Identification of Selected Drugs for Initial Price Applicability Year 2026]

¹ Association for Accessible Medicines. (September 2022). "2022 Generic and Biosimilar Medicines Savings Report." Accessible at: <https://accessiblemeds.org/resources/reports/2022-savings-report>

Under the Inflation Reduction Act (“IRA”), a product is not considered a “qualifying single-source drug” if a generic or biosimilar product is approved and *marketed*.

The IRA does not include any statutory definitions for the term “marketing.” For the initial selection year, CMS is proposing to use Part D Prescription Drug Event (“PDE”) data for the 12-month period beginning August 16, 2022, and ending August 15, 2023, to assess whether a generic drug or biosimilar product meets the “marketing” requirement. CMS further states it will seek to determine that the manufacturer of the biosimilar or generic has “engaged in bona fide marketing.”² We are concerned that this approach ignores practical challenges associated with relying solely on PDE data and is inconsistent with the statutory language within the IRA.

PDE Data would be Insufficient to Identify Generic or Biosimilar Marketing, in part, due to Part D Policies that Limit Adoption of New Generics and Biosimilars

There are numerous barriers in place throughout the Part D program design, the competitive landscape, and product safety and handling requirements that initially limit volume for generics and biosimilars as they enter a market. The proposal to use PDE data ignores these market and policy realities that can delay generic and biosimilar adoption.

For instance, some generics and biosimilars commonly face a slower adoption curve, especially in markets covering chronic diseases. In fact, many observers have pointed out that while a biosimilar adalimumab is in on the market today, and more are slated to launch this summer, there are a series of naturally occurring factors that point to why biosimilar adoption in that market may not ramp up until next year.³

Moreover, previous AAM research demonstrates how Part D formularies often delay coverage of “first generics”⁴, calling into question the proposal to exclusively rely on PDE data in order to determine whether a generic or biosimilar is “marketed. Furthermore, Part D policies do not currently permit plan sponsors to substitute reference biological products with newly launched biosimilars on their formularies at the mid-year point as a maintenance change. This represents an additional barrier for biosimilars as they seek to gain market share and bring lower costs to the healthcare system, especially within the art D program.

In June 2022, the Federal Trade Commission (“FTC”) released an enforcement policy statement outlining the legal authorities that may apply when dominant drug companies pay rebates and fees to middlemen

² Centers for Medicare and Medicaid Services (March 2023) Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (cms.gov) Accessible at: <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>

³ Matrix Global Advisors (February 2023) Near-Term Expectations for Adalimumab Biosimilars in the United States. Accessible at: https://getmga.com/wp-content/uploads/2023/02/Adalimumab_Biosimilars.pdf

⁴ Association for Accessible Medicines (July 2021) New Evidence Shows Medicare Part D Plans Continue to Fail to Get New Generics to Seniors. Accessible at: <https://accessiblemeds.org/sites/default/files/2021-07/AAM-New-Generics-Are-Less-Available-in-Medicare-2021.pdf>

that foreclose competition from less expensive generic and biosimilar alternatives.⁵ This very principle identified by the FTC is at the heart of why PDE data will not be reliable in this case. Until CMS or the FTC act to eliminate anti-competitive rebate contracts that give maximum market power to high-cost, brand drugs, PDE data cannot be exclusively used to determine if a biosimilar or generic launch meets the statutory criteria that the product is “marketed.”

Determining Marketing Status Based on Volume of Sales is Inconsistent with the IRA

To assess whether a generic or biosimilar is marketed, CMS plans to use PDE data to determine whether the generic or biosimilar has engaged in “bona fide marketing”. This implies that CMS will make the determination based on specific levels of generic or biosimilar market adoption. However, the IRA only requires a generic or biosimilar to be “marketed” and does not require that the generic or biosimilar have achieved a certain level of market penetration, either in the Medicare program or in the broader U.S. pharmaceutical environment. A requirement for “bona fide marketing” is therefore new and not found in the IRA. As such, this new requirement should not be implemented. The formal notice and comment process could have provided the agency with meaningful stakeholder input noting the inconsistency of a “bona fide marketing” requirement with the statute and helped the agency to craft a workable approach to measure “marketing” in line with the statutory requirements.

The new requirement for “bona fide marketing” appears to be an attempt to give CMS discretion to continue negotiating a brand drug’s price even after a generic or biosimilar is on the market, even though this authority was not provided by Congress. While we understand that CMS may be concerned about attempts to game the system, the statutory language is clear and such concerns are not supported by historical trends or currently available evidence. Generic and biosimilar manufacturers work aggressively to launch products quickly and successfully. During the early years of the generic market, there were similar concerns that the Hatch-Waxman Act, which established the legal framework for generic submissions, would incentivize generic manufacturers to limit the volume of products launched. But this has not been the case. Whereas pre-Hatch-Waxman only 35% of the top selling drugs had a generic available, generics now represent 91% of all prescriptions dispensed.^{6, 7}

CMS Should Use Multiple Data Sources to Determine Marketing Status

Multiple existing federal and non-federal resources already exist to answer the question of whether a generic or biosimilar is available in the marketplace. For instance, the National Institutes of Health (NIH) DailyMed publishes product marketing dates, information that is then used by CMS for Average Sales Price (“ASP”) submission verification. Furthermore, first generic applicants must notify the FDA of the date on which they commence commercial marketing.⁸

⁵ Federal Trade Commission (June 2022) FTC to Ramp Up Enforcement Against Any Illegal Rebate Schemes, Bribes to Prescription Drug Middlemen That Block Cheaper Drugs. Accessible at: <https://www.ftc.gov/news-events/news/press-releases/2022/06/ftc-ramp-up-enforcement-against-illegal-rebate-schemes>

⁶ Silver R. A Wall Street Perspective on Generics (2007) GPhA Meeting, March 1-3, 2007. Accessible at: www.gphaonline.org/AM/CM/ContentDisplay.cfm?ContentFileID=593

⁷ Association for Accessible Medicines (September 2022) The U.S. Generic & Biosimilar Medicines Savings Report. Accessible at: <https://accessiblemeds.org/sites/default/files/2022-09/AAM-2022-Generic-Biosimilar-Medicines-Savings-Report.pdf>

⁸ The FDA has the primary jurisdiction over regulating product launches and has issued regulations that include a clear and workable definition of marketing consistent with the IRA. **21 CFR § 314.3(b)** defines “commercial

In fact, it may be that there will be no single perfect source. Therefore, we encourage CMS to take a multi-faceted approach including (1) use of existing resources (market compendia such as Micromedex's RED BOOK, First Databank, Medispan, or Gold Standard; or federal sources such as DailyMed, FDA NDC directory) for marketing status, (2) allowing generic or biosimilar manufacturers to certify marketing status to the Agency on a rolling basis (including the opportunity to appeal a CMS marketing determination), and (3) as necessary, consultation of broader datasets reflecting the full U.S. pharmaceutical market, such as IQVIA, to identify sales.

As noted, this should include the opportunity for generic or biosimilar manufacturers to certify to the Agency that a generic or biosimilar has been "marketed" and to appeal a marketing determination through provision of information demonstrating that the product is available for purchase. Such an approach is consistent with the language in Appendix C of the memorandum, where the Agency specifies "marketing" is defined as the introduction or delivery for introduction into interstate commerce of a drug product.

If CMS seeks to determine information available regarding sales activity, reliance on PDE data would inappropriately narrow the opportunities for confirmation. Accordingly, any such confirmatory analysis of sales should use a broader data set, such as data from IQVIA®, IDB or other data sources, that capture near real-time transactions involving generic and biosimilars in the market as a whole.

CMS Should Allow for a "Rolling" Determination of Generic or Biosimilar Marketing

We note that the memorandum does not address when the Agency will determine whether a generic or biosimilar is marketed once the negotiation process has already started. The memorandum is clear that a selected drug will be removed from the negotiation process once the Agency determines there is generic or biosimilar availability on or after the selected drug publication date and during the negotiation period for an initial price applicability year. However, the memorandum does not outline when or how this determination will be made. For example, if a generic or biosimilar is marketed during the negotiation process (e.g., one day or three months after CMS announces the selected drugs), how and when will CMS make this determination? Creation of a pathway for generic or biosimilar manufacturers to certify marketing status is one way to immediately make a marketing determination and, if applicable, remove the reference product from the negotiation process.

CMS Should Use Alternative Data Sources to Confirm Marketing and Sales

As noted, we believe the statutory language is clear that the marketing determination does not allow for consideration of levels of adoption as a requirement. However, when verifying details of marketing through reporting generated by generic and biosimilar manufacturers, there may be no individual source that is sufficiently comprehensive. AAM urges CMS to clarify that the Agency will closely adhere to the statutory requirements outlined in the IRA with respect to making a determination of whether a

marketing" as "the introduction or delivery for introduction into interstate commerce of a drug product described in an ANDA, outside the control of the ANDA applicant, except that the term does not include transfer of the drug product for investigational use under part 312 of this chapter or transfer of the drug product to parties identified in the ANDA for reasons other than sale. Commercial marketing includes the introduction or delivery for introduction into interstate commerce of the reference listed drug by the ANDA applicant."

product is a single-source drug and will not impose additional requirements related to market share minimums. Specifically, CMS should clarify that listing in pharmaceutical compendia or in Federal resources (NIH DailyMed), a certification of marketing from the generic or biosimilar manufacturer, or the presence of *any* sales of a biosimilar and generic drug in PDE files and/or a real-time transaction data source will satisfy the IRA's statutory requirement to demonstrate that a generic or biosimilar has been marketed. We urge CMS not to impose a different, more demanding standard than what is required by statute.

CMS Should Maintain An Updated Part D Dashboard To Allow For Appropriate Evaluation Of Drug Expenditures [30.3.1.1 Requirements for Granting an Initial Delay Request for Initial Price Applicability Year 2026]

The memorandum encourages stakeholders to rely on publicly available information including the Medicare Part D Drug Dashboard to determine which products may be selected for negotiation. We would note that the most recent data available from the CMS Part D Drug Dashboard was published March 2023 using 2021 data. This represents a significant lag that undermines biosimilar developers' ability to forecast likely products for selection and submit appropriate requests for delay. Accordingly, AAM requests that the Agency update the dashboard on a more frequent timeframe or provide more recent information related to the top 50 Part D products. Alternatively, if CMS believes that other reliable data sources exist, we encourage them to identify those publicly. This will enable stakeholders, including generic and biosimilar manufacturers, to prepare for potential delay applications and ensure the Agency is aware of products that have been approved and marketed.

CMS Should Expand the Criteria for the Two-Year Delay [Section 30.3.1.2 High Likelihood]

The IRA guidance provides biosimilar applicants with only two options to demonstrate “high likelihood” of marketing, both of which require resolution of any patent disputes, either by a court decision or an agreement with the reference product sponsor, no later than May 22, 2023. This approach is unduly narrow for several reasons.

First, this approach would disqualify any 351(k) BLAs submitted after May 22, 2023 from eligibility, as patent litigation cannot commence—much less be resolved—until after application submission (*See id.* § 271(e)(2)(C)).

Applications submitted by May 22, 2023 do not fare much better, as CMS's requirements do not appropriately address the practicalities of patent litigation and the statutory requirements governing these disputes. To the extent that it is used, the “patent dance” takes approximately 250 days—and that is just before the first wave of litigation. Accordingly, for litigation to even have commenced by May 22, 2023, the biosimilar applicant must have *already* submitted its 351(k) BLA by September 14, 2022.

Second, ongoing patent litigation may be irrelevant to biosimilar launch. If, for example, a biosimilar applicant carves out the relevant patented indication from its labeling—a common practice in the biosimilar space—it may never be sued by the reference product sponsor consistent with applicable law. CMS's limited criteria provide no basis for the biosimilar applicant to demonstrate a “high likelihood” in that circumstance—despite the fact that there are no barriers precluding the biosimilar manufacturer from entering the market.

Separately, CMS's view that "active litigation" disqualifies a biosimilar manufacturer from satisfying the "clear and convincing evidence"⁹ standard is inconsistent with the statutory intent of the IRA biosimilar delay provision, and it will ultimately lead to less aggressive patent challenges. Patent litigation is inherently uncertain, fast-moving and should not be indicative of approval or marketing of a biosimilar. Under CMS' current standard, a biosimilar manufacturer that overwhelmingly establishes at trial that the relevant patents are invalid and/or not infringed upon would be ineligible for the delay—even if the decision from the district court was a mere few days away. Moreover, multiple biosimilars on the market today have launched 'at risk' during ongoing litigation, and this type of aggressive commercialization is a goal that CMS should seek to support.¹⁰

Furthermore, establishing a de facto standard that ongoing litigation disqualifies a biosimilar from receiving a two-year delay grants brand manufacturers too much control over this process, as they would have the ability to keep litigation active regardless of the willingness of a biosimilar manufacturer to launch at risk.

The IRA Includes Safeguards for Taxpayers if the Biosimilar Fails to Launch within Two Years

It is important to keep in mind that the IRA is intended to encourage generic and biosimilar competition, and that, furthermore, it provides a safeguard for situations in which a biosimilar delay is granted, but the biosimilar is not marketed. Under the IRA, if a delay is granted and a biosimilar is not subsequently marketed, a brand manufacturer will be required to pay a rebate for the years during which they would have provided access to a Maximum Fair Price (MFP). Accordingly, since there is already a defined safeguard in place to protect the negotiation program and taxpayers if a biosimilar is not launched, it is appropriate to expand the criteria for biosimilars to be eligible to receive the two-year delay. This approach will reduce uncertainty for biosimilar manufacturers as they invest in development, increase competition, and reduce prices for patients and the Medicare Program.

AAM urges CMS to alter this standard to allow biosimilars with ongoing litigation but no adverse court decision to be eligible to receive the two-year delay. Moreover, CMS could permit biosimilar manufacturers to submit explanations detailing why market entry is likely that could then be evaluated by the agency, rather than resorting to an overly restrictive test that undermines biosimilar competition.

CMS Should Ensure the Information Provided During the Biosimilar Initial Delay Request Process Remains Confidential [Section 40.2.1 Confidentiality of Proprietary Information]

CMS proposes to maintain proprietary information submitted to inform the negotiation process confidential in accordance with statutory requirements. AAM agrees that this nonpublic information should remain undisclosed. Thus, we urge CMS to clarify that information submitted as part of the Biosimilar Initial Delay Request will be exempt from Freedom of Information Act (FOIA) requests or other disclosures.

¹⁰ The following products were launched at-risk and are currently available on the market: Kanjinti (trastuzumab-anns) [July 2019], Inflectra (infliximab-dyyb) [November 2016], Fulphila (pegfilgrastim-jmdb) [June 2018], Mvasi (bevacizumab-awwb) [July 2019]

CMS Should Clarify Appropriate Maximum Fair Price and Administrative Fees [Section 40.4 Providing Access to the MFP]

The memorandum notes that, in addition to MFP-eligible individuals, manufacturers are also required to ensure that pharmacies, mail order services, and other dispensers are also able to access the selected drug at the MFP. Specifically, CMS intends to require a Primary Manufacturer to reimburse a pharmacy, mail order service, or other dispenser within 14 days if the entity does not have access to the MFP. The memorandum specifies that manufacturers or contracted entities may not charge any transaction fee for this process. We encourage CMS to also prohibit pharmacy benefit managers (PBMs) or Part D plan sponsors from charging any additional transaction or administrative fees from manufacturers or pharmacies in connection with the MFP or the selected drug dispensing process. PBMs or Part D plan sponsors should not be able to generate revenue from pharmacies or manufacturers complying with the requirements of the IRA or subsequent program rules. We have urged the agency in the past to ensure patients receive the benefit of all rebates, discounts, and direct and indirect remuneration at the pharmacy counter, and we continue to encourage CMS to ensure this occurs for products subject to the MFP as well as for all other Part D products.

CMS Should Provide Greater Clarity on the Determination of the Maximum Fair Price [Section 50 - Evidence Regarding Therapeutic Alternatives]

Although the IRA seeks to protect generic and biosimilar competition by removing a reference product from negotiation if a generic or biosimilar is approved/licensed and marketed, the framework nonetheless creates significant uncertainty that, without greater clarity from CMS, will harm future generic and biosimilar development. Generic and biosimilar manufacturers make decisions on how to direct capital investments, in relation to a reference product's market activity, years before loss of exclusivity is imminent and years before CMS will begin the negotiation process. Currently, generic and biosimilar manufacturers rely on current, publicly accessible trends in commerce and free market economics to govern how they direct their operations in bringing affordable medicines to the US healthcare system. However, the market uncertainty created by this guidance could undermine their decision to invest the \$100-\$250 million and 8-12 years necessary to bringing the lower-cost options to market in key areas such as complex generics and biosimilars. We are concerned that not providing concrete information on pricing that allows stakeholders to operate with predictability would harm long-term opportunities for greater savings through the market-based competition that biosimilars and generics offer. Accordingly, it is important for CMS to establish a predictable and transparent method for determining the MFP that allows generic and biosimilar developers to reasonably forecast the market in their investment decisions.

For instance, section 50.2 of the memorandum discusses the requirement under section 1194(e)(2) of the Act that the Secretary consider evidence regarding alternative treatments. AAM encourages CMS to provide clarity on how it will determine what constitutes a "therapeutic alternative." For instance, does CMS intend to consider the selected drug's overall place in therapy? Does CMS intend to consider drugs in other categories or classes such as those included in treatment guidelines? In considering indications for the selected drugs, does CMS intend to use a process similar to the evaluation for Medically Accepted Indication within Part D?

Likewise, the memorandum appears to envision a high degree of privacy in the actual price setting process. This is not in the public interest and will undermine the ability of generic and biosimilar

developers to reasonably support costly future development. We encourage CMS to continue to refine its approach to provide greater predictability and transparency.

Patients deserve access to more high-quality products, rather than fewer, and payers will be able to save in an environment with more competition rather than less. The uncertainty and subjectivity inherent in the approach CMS outlined in this guidance will make the process of investment in biosimilars and generics more uncertain, and risks leaving many Medicare beneficiaries and the health care system overall worse off with fewer options for care and higher costs.

CMS Should Clarify Intent of “Robust and Meaningful” Competition [Section 90.4 - Monitoring for Bona Fide Marketing of Generic or Biosimilar Product]

CMS also proposes “to monitor whether robust and meaningful competition exists in the market once it makes such a determination... [including whether it is] consistently available for purchase through the pharmaceutical supply chain.”² As noted previously, structures within the Medicare program have inhibited the increased adoption of generics and biosimilars. The intent of this provision is unclear, especially since the IRA clearly demonstrates the negotiation process is intended to encourage competition and the use of generics and biosimilars. Further, the metrics outlined for consideration within the guidance do not reflect the most appropriate method of evaluation. For instance, specialty products may not, and likely will not, be readily available in community pharmacies. And because PDE data implies formulary access and a product’s market share, this measure could be heavily weighted on factors such as long-standing branded rebate agreements with PBMs that have little to do with the effort, resources, or ability of a generic or biosimilar company to launch successfully. We encourage CMS to align coverage and payment policies with the statutory intent of the IRA by promoting approaches that increase overall adoption.

It is important to bear in mind that, as noted previously, the IRA only refers to “marketing,” not “robust and meaningful competition.” Moreover, the IRA does not include a provision for the re-introduction of a product for negotiation after a determination has been made that a biosimilar or generic has been launched and marketed nor does it include a market share threshold related to “robust and meaningful competition”. It is essential to robust and competitive biosimilar and generic markets that manufacturers have clarity on the anticipated requirements and that additional regulatory difficulties are not introduced that increase uncertainty in the launch, marketing, and introduction of new products.

Overall, we encourage CMS to exercise flexibility and collaboration during the ongoing development and implementation of the program. We look forward to continuing to engage with HHS and CMS on improving competition, care, and access for America’s patients.

Sincerely,

Craig Burton

Craig Burton
Senior Vice President, Policy & Strategic Alliances, Association for Accessible Medicines
Executive Director, Biosimilars Council



April 14, 2023

VIA ELECTRONIC DELIVERY

Dr. Meena Seshamani
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

**Re: Medicare Drug Price Negotiation Program: Initial Memorandum,
Implementation of Sections 1191 – 1198 of the Social Security Act for Initial
Price Applicability Year 2026, and Solicitation of Comments**

Dear Dr. Seshamani:

Astellas Pharma US, Inc. (Astellas) provides the following comments to the Centers for Medicare & Medicaid Services (CMS) regarding the above-referenced March 15, 2023 Initial Guidance on the Medicare Drug Price Negotiation Program (Guidance).

Astellas is an innovator company with global headquarters in Tokyo, Japan. Astellas is committed to creating innovative drugs with cutting-edge science that can address areas of high unmet medical needs. We aim to help patients who have no treatment options, or do not respond adequately to existing treatments. Astellas supports the comments of our trade association, the Pharmaceutical Research and Manufacturers of America (PhRMA), and we share PhRMA's concern that the Guidance, if finalized, would heighten the substantial risks already posed by the drug pricing provisions of the Inflation Reduction Act (IRA): curbing biopharmaceutical innovation and eroding patients' access to new therapies. We write separately to emphasize a few points of particular importance about suggestions to help mitigate the risks associated with the initial guidance. We urge CMS to work to implement the IRA's drug price-setting provisions in a way that mitigates the IRA's risks to patients, without departing from the statute's text.

Our specific comments on the Guidance can be summarized briefly as follows:

- CMS should remove tax credits from the proposed definition of prior "Federal financial support." Unlike forms of public support that CMS intends to consider when determining the preliminary price leading up to a maximum fair price (MFP), tax credits are not "Federal support" but a tool that Congress

uses to channel private investment into public policy priorities, without disbursing government funds. By using tax credits as the basis for a downward adjustment in the preliminary price, CMS would disincentivize innovation and reduce the effectiveness of tax credits as a policy tool to encourage and shape manufacturers' R&D investments.

- The revised Guidance should clarify that if prior Federal financial support is a factor that results in CMS considering a downward adjustment in a selected drug's preliminary price, any such adjustment will not exceed an amount proportional to the amount of the prior Federal financial support as a share of the total research and development investments related to the selected drug.
- To protect and promote research and development, CMS should consider an upward shift of the preliminary price for a drug with unexpired patents or exclusivities. Applying a downward adjustment would reduce the value of intellectual property rights and cause a decline in innovation, hindering critical scientific and medical advances.
- In the initial years of implementing the new MFP program, CMS should proceed carefully, with a view to reducing potential risks from the program, and set the MFP for selected drugs at or near the ceiling price to limit disruption from significant and sudden marketplace changes. After the initial period, CMS should rely on independent, consensus-driven clinical experts to assess whether a drug represents a therapeutic advance and to evaluate the comparative effectiveness of therapeutic alternatives.
- CMS should revise the Guidance to provide that CMS will publicly identify potential therapeutic alternatives to selected drugs at the earliest possible opportunity, to maximize the opportunity for all appropriate stakeholder feedback, including from manufacturers as well as clinicians who use CMS' identified alternatives in patient care.
- Consistent with the IRA targeting "single source" drugs for price-setting, and to reduce the possibility of new generics or biosimilars having to compete with MFP-priced selected drugs, CMS should remove a selected drug from the MFP program if an approved generic or biosimilar is marketed at any point before the start of the initial price applicability year (including after the

statutory “negotiation period” but before the start of the initial price applicability year).

- Finally, CMS should determine when a generic or biosimilar product is “marketed” using the commonly understood meaning of that term, instead of limiting what counts as “marketing” based on concepts at odds with the IRA and the ordinary meaning of “marketing.”

1. CMS Should Not Discourage Innovation and Reduce the Effectiveness of Tax Credits By Categorizing Them as “Federal Financial Support” (Section 50.1; Appendix C).

The IRA lists five groups of “manufacturer-specific” data elements that manufacturers of selected drugs must submit to CMS, one being “prior Federal financial support for novel therapeutic discovery and development with respect to the drug.”¹ The Guidance proposes that CMS would consider “the extent to which the Primary Manufacturer benefitted from Federal financial support,” and in particular “may consider adjusting the preliminary price downward if funding for the discovery and development of the drug was received from federal sources.”² CMS would define “prior Federal financial support for novel therapeutic discovery and development” referring to “tax credits, direct financial support, grants or contracts, and any other funds provided by the federal government that support discovery, research, and/or development related to the selected drug.”³

This definition goes beyond “prior Federal support for novel therapeutic discovery and development” with respect to the selected drug. To align with the statutory language, CMS should limit consideration to funding that directly resulted in a patent application containing a Government Interest Statement and/or research where a patent assignee was a U.S. government agency. At a minimum, though, CMS should remove tax credits from the definition.

Using prior tax credits as a basis for considering a downward adjustment in a selected drug’s preliminary price is a patently misguided policy that may have the unintended effect

¹ Social Security Act (SSA) § 1194(e)(1)(C).

² Guidance at 53.

³ Guidance at 87-88.

of limiting the impact of future tax credits—reducing the effectiveness of a key tool that Congress uses to encourage manufacturers to use their own funds in a way that advances critical public policy goals, such as investing in the research and development of new therapies to treat life-threatening and otherwise serious diseases, including therapies to treat rare diseases and, thus, address unmet patient needs. CMS' proposal would essentially undo incentives that Congress had purposely put into place. It would be counterproductive for CMS to use its MFP authority to take away explicit statutory incentives for companies to invest in medical advances.

Moreover, unlike the other specific categories that CMS proposes including in its definition of “prior federal financial support,” tax credits are not “Federal support” at all. They are in no way equivalent to government funding. Congress has long used tax credits to spur companies to increase their own investment in areas of research that may not otherwise be sustainable or otherwise would be carried out at a level inadequate to meet public health goals. Just as the IRA uses tax credits to incentivize energy-efficient purchases that consumers may not otherwise buy, Congress similarly employs tax credits to channel private sector funds into the development of therapies and cures that may not otherwise be developed. By using tax credits as part of its calculus to adjust preliminary MFPs downward, CMS would be diluting the effectiveness of this tool for boosting private spending on important medical innovations. Accordingly, we urge CMS to remove tax credits from its definition of “prior federal financial support.”

2. CMS Should Not Disproportionately Weigh Federal Financial Support In Developing Offers (Section 50.1).

As noted above, the Guidance provides that CMS will consider “the extent to which the Primary Manufacturer benefitted from Federal financial support” and “may consider adjusting the preliminary price downward if funding for the discovery and development of the drug was received from federal sources.”⁴ Other than referring to “the extent to which the Primary Manufacturer benefitted from Federal financial support,” the Guidance does not discuss how much weight CMS might give to prior Federal financial support.

We recommend that CMS look at Federal financial support in the context of the total R&D costs incurred for the selected drug and consider – at most – a proportional adjustment in the preliminary price. For example, if prior federal financial support represented 1% of the total investment required to develop a new drug, to the extent CMS considers adjusting the

⁴ Guidance at 53.

preliminary price downward as a result of such funding, it should do so in a proportional manner by adjusting the preliminary price downward by no more than 1%.

3. CMS Should Not Penalize Manufacturers for Patents and Exclusivities (Section 50.1; Appendix C).

As currently proposed, CMS “intends to consider the length of the available patents and exclusivities before the drug may no longer be single source” and may consider adjusting the preliminary price downward if the drug has patents and exclusivities that will last for a number of years.⁵ We strongly believe this proposal is ill-advised, and we urge CMS to refrain from penalizing manufacturers for patents and exclusivities. Patents and exclusivities encourage and incentivize research and development and other investment in new drugs and therapies. Post-approval R&D that could result in additional patients and exclusivities can improve patients' lives via meaningful improvements in existing therapies. Instead of undermining manufacturers' intellectual property rights and reducing motivation to improve existing therapies and/or develop groundbreaking therapies, CMS should take exactly the opposite approach.

The important role of patents in promoting scientific advancement is long-established and recognized on our Constitution. Article I of the U.S. Constitution provides for Congress “[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.”⁶ By proposing to adjust a preliminary price downward because a product has available patent rights and exclusivities, CMS would penalize manufacturers for innovation and – again – undo incentives that Congress created intentionally and for important reasons. Intellectual property rights have helped to fuel the country's leadership in global innovation for over 200 years and by using those rights as a trigger to reduce the preliminary price of a selected drug, CMS would be directly reducing the value of those intellectual property rights. This would set a troubling precedent -- contravening long-standing policies stated in our Constitution to promote intellectual property rights and spur scientific advancement.

To encourage future research and innovation, and to ensure that development continues to take place domestically, CMS should reconsider its Guidance and instead should adopt a

⁵ Guidance at 53.

⁶ U.S. Constitution, Article I, Section 8, Clause 8.

policy of rewarding innovation and adjusting the preliminary price upward for a selected drug with unexpired patents or exclusivities.

4. CMS Should Set the MFP at or Near the Ceiling Price at the Start of the Program and In Later Years Should Rely on Independent Medical Experts to Determine A Drug’s Relative Therapeutic Value (Section 60).

Given the novelty and complexity of the MFP program, and the consequences it may have across the healthcare system, CMS should proceed carefully and set the MFP for selected drugs at or near the ceiling price for at least the first several “initial price applicability years” (IPAYs). To do otherwise—on such a short timeframe and without previous experience in operating a program like this—will risk undervaluing critical drugs and potentially harming patients. To reduce risks of harm in the program’s early years, it will be important for CMS to set MFPs of selected drugs at or very close to their ceiling price, which already reflects a substantial discount on a selected drug’s pricing.

In later years, CMS should follow the guidance and experience of third-party clinical experts when considering “[t]he extent to which such drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives” as required by SSA § 1194(e)(2)(A). In the area of oncology, an important third-party expert organization is the National Comprehensive Cancer Network (NCCN). The NCCN is a not-for-profit alliance of 33 leading cancer centers devoted to patient care, research, and education that is dedicated to improving and facilitating quality, effective, equitable, and accessible cancer care so all patients can live better lives.⁷ For the past 15 years, the NCCN Drug and Biologics Compendium has been relied on as an authoritative, scientifically based source for providers when evaluating patients’ treatment options. When CMS considers evidence about alternative treatments to a selected cancer drug, including the extent to which the selected drug represents a therapeutic advance and the comparative effectiveness of the selected drug and its therapeutic alternatives, it is critical that CMS defer to experts, like the NCCN, to evaluate advances in cancer care.

The NCCN Drug and Biologics Compendium is updated on a regular basis to reflect currently available evidence. The Compendium categorizes drugs and biologics into four

⁷ See National Comprehensive Cancer Network. “About,” available at <https://www.nccn.org/home/about>; National Comprehensive Cancer Network. “NCCN Drugs & Biologics Compendium,” available at <https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia>.

categories by evaluating each treatment's efficacy and patient safety.⁸ The highest potential recommendations contained in the NCCN Drug and Biologics Compendium are defined as follows:

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate; and
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Oncology drugs (and biologics) that receive a recommendation of either Category 1 or 2A from the NCCN represent a significant therapeutic advance given that such treatments are supported by strong clinical evidence and the support of respected oncology experts. Relying on NCCN recommendations to determine “[t]he extent to which such drug represents a therapeutic advance as compared to existing therapeutic alternatives” will help to ensure that CMS’ decision making is based on sound and consensus-driven science and that manufacturers are incentivized to continue developing oncology drugs that meet the criteria to be considered a Category 1 or 2A therapy, promoting efficacy and patient safety. CMS should recognize an oncology drug that achieves one of these ratings as a significant therapeutic advance, and accordingly should set the MFP for drugs that receive these designations in the NCCN Compendium at their statutory ceiling price.

5. CMS Should Defer to Experts In Determining Therapeutic Alternatives, and Publicly Identify All Therapeutic Alternatives Considered when Setting the MFP (Section 60)

In determining the therapeutic alternatives to a selected drug, CMS should rely on clinicians with disease-specific expertise, manufacturers, and independent, widely respected experts. These groups are best positioned to know which products are potential therapeutic equivalents to a selected drug that are appropriate for consideration. For example, when CMS identifies therapeutic alternatives to a selected cancer drug, CMS should consult oncologists, the NCCN Drug and Biologics Compendium, and relevant manufacturers of oncology drugs.

Moreover, to ensure transparency, and to allow for feedback from clinicians with disease-specific and other relevant expertise, including manufacturers and independent, widely

⁸ See National Comprehensive Cancer Network. “Definitions for NCCN Categories,” available at <https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines>.

respected experts, CMS should publicly identify all therapeutic alternatives to a selected drug as early as possible in the process. Given the specialized knowledge and experience required to identify appropriate therapeutic alternatives to oncology drugs in particular, CMS should ensure that it will timely receive input from all relevant stakeholders, and that it structures its MFP-setting process so as to create multiple opportunities for stakeholders with expertise to provide feedback to CMS on therapeutic alternatives.

6. CMS Should Revise the Guidance to Remove a Selected Drug From the Program After the Negotiation Period If a Generic or Biosimilar is Approved and Marketed Before the Start of the IPAY (Section 70).

Under the IRA, a selected drug will not be subject to an MFP if CMS determines that the generic or biosimilar for the product is approved and “marketed” before the end of the statutory “negotiation period.”⁹ Given the obvious purpose of this provision—to take out of the MFP program drugs and biologics that face competition from a generic or biosimilar before their MFPs take effect, as they no longer represent “qualifying single source drugs”—CMS should also remove a selected drug from the MFP program if marketing of the approved generic or biosimilar begins after the “negotiation period” ends but before the start of the IPAY (i.e., between August 1, 2024 and December 31, 2025, for IPAY 2026).

Congress intended that the program allow for price setting for single source products. If CMS does not remove a selected drug from the program even in a case where a generic drug or a biosimilar is approved and marketed before MFPs take effect (at the start of the IPAY), this could have the unintended effect of forcing a generic drug or a biosimilar to compete with an MFP-priced listed or reference product for a year—distorting competition and undermining the program. The MFP may set a price below the level of economic viability for the generic or biosimilar competitor and undercut the ability of the generic or biosimilar to establish a stable footing in the marketplace. But under the Guidance, a generic or biosimilar that is approved and marketed during the 18-month period after the end of the “negotiation period” (ending August 1, 2024) and before the start of IPAY 2026 (January 1, 2026) would face an MFP-priced listed or reference drug for all of 2026. To avoid this outcome and the detrimental impact it could have on competition, we urge CMS to remove a selected drug from the MFP program if a generic or biosimilar for the drug is approved and marketed at any point prior to the start of IPAY, even if marketing of the generic or biosimilar product begins after the statutory “negotiation period” has ended.

⁹ See SSA § 1192(c)(2).

7. The Concept of “Bona Fide Marketing” Is Inconsistent with the IRA and Should be Removed From the Guidance (Section 90.4).

In the Guidance, CMS introduces a concept of “bona fide marketing” that is not mentioned in the statute and runs contrary to the statute. Further, this approach provides no predictability about when CMS would determine that a drug is “marketed.”

The statute defines a qualifying single source drug (QSSD) in relevant part as a drug lacking a generic or biosimilar product that is approved and “marketed.”¹⁰ The Guidance instead creates a new term -- “bona fide marketing” -- and states that “for the purpose of identifying [QSSDs] for [IPAY] 2026, CMS will review PDE [prescription drug event] data for a given generic drug or biosimilar biological product during the 12-month period beginning August 16, 2022 and ending August 15, 2023, using PDE data available on August 16, 2023, and will consider a generic drug or biosimilar biological product to be marketed when that data reveal that the manufacturer of that drug or product has engaged in bona fide marketing of that drug or product.”¹¹ The addition of the term “bona fide” -- like the plan for CMS to base its determination of whether a generic or biosimilar is marketed solely on Part D PDE data, apparently shutting out all other evidence of marketing -- are new limitations that do not appear in the IRA and conflict with the ordinary meaning of “marketed.” The Guidance also states that after CMS makes a determination that an approved generic or biosimilar is marketed, CMS “intends to monitor whether robust and meaningful competition exists in the market.” Guidance at 67. This “monitoring of competition” function also is not mentioned in the IRA and should be eliminated from the CMS guidance.

In fact, in Appendix C to the Guidance (“Definitions for Purposes of Collecting Manufacturer-Specific Data”), CMS defines “marketing” as “the introduction or delivery for introduction into interstate commerce of a drug product.”¹² This definition is consistent with the ordinary meaning of “marketing.” In its recent Part D Inflation Rebate Guidance, for example, CMS stated that “the date that the drug is first marketed would be the date that the manufacturer reports for the drug as its ‘market date’ to the Medicaid Drug Rebate Program,”¹³ which

¹⁰ SSA § 1192(e)(1)(A)-(B).

¹¹ Guidance at 10 (emphasis added).

¹² Guidance at 82.

¹³ CMS February 8, 2023 Part D Inflation Rebate Guidance at 15 n.18. See also id. at 19 (“to identify the ‘first marketed’ date [for a new drug], CMS intends to use the market date that the manufacturer is required to report under [SSA] section 1927(b)(3)(A)(v)”).

defines a “marketed” drug as a drug that “is available for sale by a manufacturer in the states.”¹⁴ Further, the definition in Appendix C and in the Medicaid rebate guidance aligns with FDA’s use of the term “marketing.” For example, in the context of 180-day exclusivity for first generic applicants, the Food, Drug, and Cosmetic Act (FDCA) provides that FDA shall not make effective a subsequent generic application until “180 days after the date of the first commercial marketing of the drug . . . by any first applicant.”¹⁵ FDA regulations define the term “commercial marketing” (which is more narrow than “marketing”) as “the introduction or delivery for introduction into interstate commerce of a drug product described in an ANDA.”¹⁶ Similarly, for purposes of FDCA section 506l on marketing status reports, FDA considers a product’s marketing status to depend on whether the product is distributed by the application holder, i.e., whether the product is available for sale.¹⁷ Dictionary definitions of marketing reflect the same understanding of this term.¹⁸ Thus, FDA’s definitions and CMS’ own definitions -- in its Medicaid rebate program guidance, in its inflation rebate guidance, and in Appendix C to this Guidance -- and dictionary definitions all reflect the generally accepted ordinary meaning of “marketing” a pharmaceutical product, and thus the meaning of “marketed” that Congress intended in the context of the IRA.¹⁹ By contrast, the reference in the Guidance to “bona fide” marketing, and its description of how

¹⁴ Medicaid National Drug Rebate Agreement, Section (I)(1).

¹⁵ 21 U.S.C. § 355 (j)(5)(B)(iv)(I).

¹⁶ 21 C.F.R. § 314.3.

¹⁷ FDA, Guidance for Industry, [Marketing Status Notifications Under Section 506l of the Federal Food, Drug, and Cosmetic Act; Content and Format](#), at 3 (Aug. 2020) (describing the discontinuation of marketing a product as ceasing distribution).

¹⁸ For example, Merriam-Webster’s dictionary defines “market” (transitive verb) as “to expose for sale in a market” or “sell.” Merriam-Webster.com. 2023. <https://www.merriam-webster.com> (April 9, 2023). Black’s Law Dictionary similarly defines marketing as “the act or process of promoting and selling, leasing, or licensing products or services.” Black’s Law Dictionary (11th ed. 2019).

¹⁹ See, e.g., *Asgrow Seed Co. v. Winterboer*, 513 U.S. 179, 187–88 (1995) (holding that where the statute at issue did not define “marketing,” the term’s “ordinary meaning” -- “the act of holding forth property for sale, together with the activities preparatory thereto” -- should apply because it is consistent with the dictionary definition, and noting that the “word [marketing] does not require that the promotional or merchandising activities connected with the selling be extensive”); see also, e.g., *U.S. v. Lopez*, 590 F.3d 1238 (11 Cir. 2009) (explaining that “[w]hen a statutory term is undefined, courts give it its ‘ordinary meaning’ or ‘common usage,’” and that “[t]o ascertain ordinary meaning, courts often turn to dictionary definitions for guidance”) (internal citations omitted).

CMS plans on determining whether a generic or biosimilar is marketed (i.e., by focusing exclusively on Part D PDE data) have no statutory foundation.

The statute does not require or authorize CMS to consider PDE data in assessing the marketing status of a generic or biosimilar, let alone allow CMS to ignore all other sources of marketing information. Relying exclusively on PDE data to determine when a generic or biosimilar is marketed is inappropriate. PDE data only reflects Part D claims: Part D plans are a subset of payors, which themselves are a subset of the larger biopharmaceutical marketplace, and a subset that pays for newly-approved drugs later than other segments of the pharmaceutical marketplace. And Medicare Part D plans are “notably slower than commercial plans in coverage of first generics. . . . For the 2021 Medicare Part D plan year, on average, only 21% of first generics that launched in 2020 were covered by plan formularies.”²⁰ Further, the same analysis by the Association for Accessible Medicines found that “it takes nearly three years before first generics are covered on more than half of Medicare Part D formularies.”²¹ This delayed utilization pattern is consistent with the fact that CMS allows Part D plans’ Pharmacy and Therapeutics Committees a lengthy period to review new drugs and decide whether to place them on formulary.²² In short, relying solely on PDE data to determine when a new generic or biosimilar is marketed is an arbitrary and irrational approach that inevitably will miss most of the evidence on marketing and determine an incorrect date for when marketing of the product began.

CMS should remove the concept of “bona fide marketing” and the planned reliance on PDE data from the Guidance. CMS should determine whether a product is “marketed” based on the common understanding of that term, not based on a strangely narrow concept of marketing that would shut out all evidence of marketing activities except whatever PDE data may “reveal.” CMS’ Part D Inflation Rebate Guidance suggests a simple way to determine when a drug is marketed: “the date that the drug is first marketed would be the date that the

²⁰ Association for Accessible Medicines (AAM), New Generics are Less Available in Medicare than Commercial Plans: New Evidence Shows Medicare Part D Plans Continue to Fail to Get New Generics to Seniors (July 2021).

²¹ AAM, New Generics are Less Available in Medicare than Commercial Plans: New Evidence Shows Medicare Part D Plans Continue to Fail to Get New Generics to Seniors, supra.

²² Medicare Prescription Drug Benefit Manual, chap. 6, section 30.1.5 (Part D plans’ P&T committees should generally make a “reasonable effort” to review a newly-approved drug within 90 days and decide whether to add the drug to the plan formulary within 180 days, or provide a “clinical justification” for not meeting this timeframe); section 30.2.5 (even for new drugs in the Part D six protected classes, plan P&T committees have 90 days to review the new drug and add it to the plan’s formulary).

manufacturer reports for the drug as its 'market date' to the Medicaid Drug Rebate Program."²³ We urge CMS to rely on that simple approach, which is consistent with defining marketing as "the introduction or delivery for introduction into interstate commerce of a drug product"²⁴ in accordance with its ordinary meaning.

* * *

We thank CMS for the opportunity to comment on this very important matter. We hope that CMS will take our feedback, as well as that of PhRMA, into consideration as it revises the Guidance to ensure it conforms with the statute and ultimately provides the best environment for patients to access novel medicines. If you have any questions, please do not hesitate to contact Emily Baron at emily.baron@astellas.com.

Sincerely,

A handwritten signature in cursive script that reads "Emily Baron".

Emily Baron

Senior Director, Policy Management & Analysis

²³ CMS February 8, 2023 Part D Inflation Rebate Guidance at 15 n. 18, 19.

²⁴ Guidance, Appendix C.

April 14, 2023

Meena Seshamani, M.D., Ph.D
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health & Human Services
7500 Security Boulevard
Baltimore, MD 21244-1850

**RE: Medicare Drug Price Negotiation Program: Initial Memorandum,
Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price
Applicability Year 2026, and Solicitation of Comments**

Dear Deputy Administrator Seshamani,

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialization of prescription medicines, primarily for the treatment of diseases in three therapy areas – Oncology, Cardiovascular, Renal & Metabolism (CVRM) and Respiratory & Immunology. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide.

AstraZeneca appreciates the opportunity to submit comments in response to the above captioned guidance (the “Guidance”) setting forth the Centers for Medicare & Medicaid Services' (CMS's) proposed policies for implementing the Medicare Drug Price Negotiation Program (Negotiation Program) for initial price applicability year (IPAY) 2026. We have provided comments regarding the Guidance in a section-by-section format, below. Our key areas of focus can be summarized as follows:

- **AstraZeneca appreciates CMS's recognition of Congressional intent to exclude orphan drugs from the Negotiation Program as well as CMS's request for feedback about how to best preserve the orphan drug development pipeline. AstraZeneca urges CMS to support orphan drug development by clarifying that, in the context of an orphan drug, the 7- or 11-year period that must elapse before a drug can be considered for negotiation begins upon the date that the orphan drug exclusion no longer applies.** CMS should issue additional guidance to clarify that the orphan drug exclusion entirely insulates a product (including any revenues) from the IRA's negotiation provisions for the entire duration the exclusion applies. Notably, the orphan drug exclusion constitutes a threshold exclusion from the definition of a QSSD. It must follow from this structural placement that the 7- or 11-year pre-negotiation period that would otherwise apply to a QSSD is *tolled* until the first day after the orphan drug no longer meets the requirements of the orphan drug exclusion. This approach will better enable innovator

companies to initially pursue orphan indications by initiating the pre-negotiation period only upon a subsequent approval for a distinct disease or condition. We appreciate CMS's focus on the importance of orphan drugs to the patients who need them and support CMS implementing policies that recognize and considers the individual contributions of each orphan indication as it evaluates Medicare spending and other negotiation factors.

- **To preserve the incentive structure established by the Orphan Drug Act (ODA), AstraZeneca also asks CMS to exclude from negotiation any product for which all indications, in the aggregate, treat fewer than 200,000 patients in the United States.** The express purpose of the ODA is to encourage the development of innovative pharmaceutical products to treat diseases and conditions with very small patient populations, defined by Congress as those affecting fewer than 200,000 persons in the United States. While the IRA includes an orphan drug exclusion, evincing a clear intent to preserve Congress' longstanding support and incentives for drugs treating small patient populations, namely populations of fewer than 200,000 patients, CMS's proposed approach to implementing this exception fundamentally disrupts this purpose by leaving unprotected rare disease therapies that treat fewer than 200,000 patients even across multiple indications.
- **AstraZeneca supports CMS's approach to ranking and selecting drugs based on Total Expenditures.** We support the approach laid out in Section 30.2 for identifying the 50 qualifying drugs with the highest Total Expenditures during the applicable 12-month period and the approach under Section 30.3 for selecting the 10 highest-ranking negotiation-eligible drugs for negotiation in rank order.
- **AstraZeneca urges CMS to take a multi-faceted approach to considering a selected drug's clinical value.** While AstraZeneca appreciates that CMS is required by statute to take into consideration certain manufacturer-specific factors in setting the maximum fair price (MFP) for a selected drug, we note that such factors are to be considered only "as applicable to the drug" and not all of the statutory negotiation factors must be weighted equally. An unbalanced reliance on specific factors may result in an arbitrary pricing methodology. We recommend that CMS replace its proposed approach with one that is multifaceted and accounts for the clinical value of a product using 5 key principles (outlined below). We also encourage CMS to implement an MFP methodology that provides the MFP ceiling price for medicines that either treat conditions with an unmet need or represent a significant therapeutic advance.
- **AstraZeneca urges CMS to provide a more detailed framework regarding how the agency intends to consider therapeutic alternatives and evaluate comparative effectiveness, and to engage manufacturers of selected drugs regarding the selection of therapeutic alternatives.** While CMS outlines a flexible approach to considering therapeutic alternatives and evaluating comparative effectiveness, there are numerous open

questions that warrant CMS engaging the selected drug manufacturer regarding the methodology.

- **AstraZeneca supports CMS’s policy of not considering QALYs for purposes of the Negotiation Process, which is consistent with the plain statutory language of the IRA.** We similarly support the agency's scrutiny of any comparative effectiveness research that may rely on QALYs for its conclusions.

Below, we describe each of the above comments in greater detail, in the order they appear in the guidance, and offer additional recommendations for CMS’s consideration:

I. Section 30: Identification of Selected Drugs for Initial Price Applicability Year 2026

AstraZeneca understands that CMS is issuing Section 30 of the Guidance in final form without an opportunity to comment. However, AstraZeneca is concerned that CMS is moving forward with policies that significantly reshape the way drugs are priced in the Medicare program without providing the public with the opportunity for comment, particularly because some of the policies described in Section 30 exceed the agency's statutory authority, and others pose significant policy or operational concerns that the agency may not have considered. AstraZeneca is therefore submitting comments on Section 30 and urges CMS to consider these comments as the Agency implements the Negotiation Program.

A. CMS's “qualifying single source drug” definition is overly broad and not supported by the statute. (Section 30.1)

CMS is defining the term “qualifying single source drug” (QSSD) broadly to include all dosage forms and strengths of the drug with the same active moiety (or for biologics, active ingredient) and the same holder of the New Drug Application (NDA) (or for biologics, Biological License Application (BLA)), inclusive of products that are marketed pursuant to different NDAs or BLAs.

CMS’s QSSD definition is overly broad and not supported by the statute. Section 1192(e)(1) of the Act outlines the definitional criteria for QSSDs. For both small-molecule drugs and large-molecule biological products, the statute unambiguously anchors the QSSD definition to the *singular* approval by the Food and Drug Administration (FDA) under which the product is marketed.¹ The statute in no way authorizes CMS to convert the statute's focus on a *singular* FDA

¹ For drugs to be a QSSD, section 1192(e)(1) of the Act requires only that the drug be “approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act and is marketed pursuant to such approval.” Likewise for biological products, section 1192(e)(2) requires only that the biological product be “licensed under section 351(a) of the Public Health Service Act and is marketed under section 351 of such Act.” Canons of statutory construction suggest that a legislative drafter writes precisely and in accordance with the rules of grammar. *See, e.g.,* *Arcadia v. Ohio Power Co.*, 498 U.S. 73, 79 (1990) (“In casual conversation, perhaps, such absent-minded duplication and omission are possible,

approval to a definition that sweeps in products with multiple separate FDA approvals through the addition of an “active moiety/ingredient” test. As such, the term QSSD should be defined no more broadly than the NDA/BLA, which is the approval under which the product is originally marketed.

CMS’s reliance on section 1192(d)(3)(B) of the Act to support its aggregation of NDA/BLAs in identifying QSSDs is misplaced because it ignores sequential placement of the QSSD definition relative to the “total expenditures” calculation. Section 1192(d)(3)(B) of the Act describes the aggregation of *dosage forms and strengths* for purposes of calculating Parts B and D total expenditures to determine whether a drug that is *already* a QSSD qualifies as a “negotiation-eligible” drug. Section 1192(d)(3)(B) does not govern the identification of the underlying QSSD. Stated differently, section 1192(d)(3)(B) applies *after* the QSSD is identified and ensures that the different dosage forms and strengths of a QSSD are incorporated into the total expenditure calculation. This requirement is intended to account for the common circumstance where a single NDA/BLA, and even a single supplemental NDA/BLA, can have multiple dosage forms and strengths.

Additionally, CMS’s aggregate approach to defining QSSD may stymie innovation and limit patient access to new therapies that could improve their health outcomes. Pursuing FDA approval for a new product affords patient access to new scientific advances, including products that are easier to administer, have fewer side effects, or treat new indications.² However, obtaining such approval involves a significant expenditure of resources, even if the new product shares the same active ingredient/moiety with an existing therapy. If CMS aggregates separate NDAs/BLAs into a single QSSD, manufacturers will be deterred from making investments that would otherwise advance the scientific understanding of disease states and bring new scientific applications to bear for patients.

- B. AstraZeneca supports CMS’s proposal that a generic/biosimilar for “any of the strengths or dosage forms of the potential qualifying single source drug” would disqualify the drug/biological product from the QSSD definition. (Section 30.1)

CMS states that “[i]f any strength or dosage form of a potential qualifying single source drug is the listed drug or reference product, as applicable, for one or more generic or biosimilar biological products that CMS determines are approved and marketed . . . the potential qualifying

but Congress is not presumed to draft its laws that way.”) Thus, Congressional reference to only a singular approval should be given weight. *See, e.g., Niz-Chavez v. Garland*, 141 S. Ct. 1474, 1480 (2021) (emphasizing the use of “the singular article ‘a’” to conclude that the statute referred to a singular term).

² For instance, we received NDA approval from FDA in 2014 for LYNPARZA (Olaparib) capsules, which had a recommended dosage of 8 capsules per day. Following subsequent research and development, we received a separate NDA approval from FDA in 2017 for LYNPARZA (olaparib) tablets, which formulation reduced the recommended dosage to 2 tablets per day. As another example, CALQUENCE launched a new formulation in 2022, which now allows for co-administration with proton-pump inhibitors. And FASENRA launched a new method of administration in 2019—an autoinjector that can be administered by a patient or caregiver following proper training and if the healthcare provider deems it appropriate.

single source drug will not be considered a qualifying single source drug for initial price applicability year 2026.”³

While AstraZeneca opposes CMS’s QSSD definition, to the extent CMS proceeds with such an overly expansive interpretation, AstraZeneca would support CMS’s policy position in relation to the impact of generic/biosimilar competition on a QSSD. Specifically, since CMS’s QSSD definition is so broad, it is necessary (as a limiting principle) that a generic/biosimilar for *any* of the branded product’s strengths and/or dosage forms is a sufficient condition to disqualify the potential QSSD, particularly because generic/biosimilar manufacturers may not seek approval for all of the strengths or dosage forms of the branded product. However, we have some concerns regarding CMS’s proposal with respect to confirming the presence of “bona fide” marketing of the generic or biosimilar product, as outlined in greater detail in our comments in response below to Section 90.4.

C. CMS should support orphan drug development and access. (Section 30.1.1)

CMS proposes to interpret the orphan drug exclusion under section 1192(e)(3)(A) of the Act as applying to a drug or biological product that must (1) be designated as a drug for only one rare disease or condition under section 526 of the Food, Drug & Cosmetics (FD&C) Act and (2) be approved by the FDA only for one or more indications within such designated rare disease or condition.⁴ As described in the Guidance, all dosage forms and strengths and different formulations of the QSSD must meet the criteria for the exclusion.⁵ CMS would then use the FDA’s Orphan Drug Product designation database and approvals on the FDA website to identify a qualifying orphan drug. Importantly, CMS states that it is “considering whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development.”⁶

As described below, developing drugs for orphan diseases and rare cancers is an exceedingly challenging proposition and many orphan diseases still lack an approved therapy. It is therefore essential that CMS implement the IRA’s orphan drug exclusion in a manner that encourages the continued development of orphan therapies, consistent with the intent of the Orphan Drug Act.

- i. *Developing drugs for orphan diseases is an exceptionally costly effort that poses unique challenges, but often paves the way for therapeutic advance.*

While each rare disease affects a relatively limited patient population, in the aggregate, rare diseases affect a significant number of Americans. There are approximately 30 million

³ Guidance at 10.

⁴ Guidance at 11.

⁵ *Id.*

⁶ *Id.* at 11.

people living with over 7,000 rare diseases (including rare cancers) in the United States, including millions of Medicare beneficiaries.⁷ Many of these rare diseases are debilitating and costly, negatively affecting the quality of life not only for the patients but their families and caregivers.⁸ Rare cancer conditions, which are further subdivided into many orphan sub-types, are particularly devastating and are estimated to represent a quarter of all cancer deaths.⁹ Further, supporting orphan drug development is a health equity issue. According to the National Institutes of Health, Black Americans have higher death rates for many cancer types, Hispanic and Black women have higher rates of cervical cancer, and American Indians/Alaska Natives have higher death rates from kidney cancer.¹⁰

Although there has been a significant increase in the number of drugs approved to treat rare diseases since the ODA was enacted 40 years ago, over 90 percent of known rare diseases still do not have a treatment. This is due, in part, to circumstances unique to rare diseases that further complicate the extremely costly¹¹ and high-risk¹² drug-development process.

The FDA Oncology Center for Excellence (OCE) has outlined some of the challenges to developing drugs to treat rare cancers.¹³ For example, it can be challenging to enroll a sufficient number of patients in clinical trials for rare diseases given small patient numbers, uneven distribution of disease across populations, and heterogeneity of diseases (e.g., subtype, states, and exposure to prior treatment). It is similarly challenging to design clinical trials for rare disease populations given difficulties designating an appropriate comparator, validating novel endpoints, and obtaining sufficient data from small patient populations. Obtaining the high-quality data necessary to evaluate the clinical trial outcomes for orphan diseases is also a challenge given diversity in clinical presentation, disease progress, and other patient characteristics. In addition, there may be limited or lack of timely access to molecular testing to determine eligibility for treatment with targeted therapies.

Meanwhile, because many rare disease drugs are the first and/or only products for a given disease, rare diseases lend themselves to being a starting point in the translation of new scientific

⁷ G. Yang et al. The national economic burden of rare disease in the United States in 2019, *Orphanet J. Rare Dis.* 17:163 (2022), pp. 1-11.

⁸ *Id.* (finding that over half of the \$966 billion economic burden of rare disease were indirect and nonmedical costs for patients and families).

⁹ “About Rare Cancers”, National Cancer Institute (last updated February 27, 2019), <https://www.cancer.gov/pediatric-adult-rare-tumor/rare-tumors/about-rare-cancers>.

¹⁰ “Cancer Disparities”, National Cancer Institute (last updated March 28, 2022), <https://www.cancer.gov/about-cancer/understanding/disparities>.

¹¹ The cost of the drug development process has been estimated to take 10 to 15 years and \$1-2 billion. I.V. Hinkson, B. Madej, E.A. Stahlberg. Accelerating therapeutics for opportunities in medicine: a paradigm shift in drug discovery *Front Pharmacol*, 11 (2020), p. 770. (defining the cost of the drug development process to include all costs borne by a manufacturer leading up to FDA-approval or a particular drug).

¹² Ninety percent of clinical trials for candidate drugs ultimately prove unfeasible. H. Dowden, J. Munro. Trends in clinical success rates and therapeutic focus *Nat Rev Drug Discov*, 18 (2019), pp. 495-496.

¹³ FDA, OCE Rare Cancers Program, <https://www.fda.gov/about-fda/oncology-center-excellence/oce-rare-cancers-program> (last accessed April 4, 2023).

discoveries to clinical medicine. As data emerge, drug manufacturers sometimes identify promising new uses for existing orphan therapies – in many cases for additional orphan indications. In addition to identifying patient needs and scientific pathways, there needs to be a business case for making this investment since the exploration of new indications requires significant resources. Indeed, one of the challenges OCE highlights with respect to the development of drugs for rare cancers is “[d]ecreased financial incentives for drug development.”¹⁴

- ii. *We appreciate CMS’s focus on the importance of orphan drugs to patients who need them and support CMS implementing policies that recognize and evaluate the individual contributions of each orphan indication as it evaluates Medicare spending and other negotiation factors for orphan products. AstraZeneca believes that CMS can take additional actions to “best support orphan drug development” as it relates to the implementation of the orphan drug exclusion, including by excluding drugs from the Negotiation Program that treat indications with a collective total of fewer than 200,000 patients to preserve the incentives for orphan drug development created by Congress in the Orphan Drug Act.*

The stated purpose of the ODA, as enacted by Congress in 1983, is to “provide financial incentives” to manufacturers for diseases and conditions “which affect such small numbers of individuals residing in the United States.”¹⁵ Specifically, the express purpose of the ODA is to encourage the development of innovative pharmaceutical products to treat diseases and conditions with very small patient populations, defined by Congress as those affecting fewer than 200,000 persons in the United States.¹⁶ The FDA, the agency with direct oversight of this program, recognizes this clear purpose, noting that it is challenging to create treatments and cures for rare diseases, including “...the complex biology and the lack of understanding of the natural history of many rare diseases. The inherently small population of patients with a rare disease can also make conducting clinical trials difficult.”¹⁷

In passing the IRA, Congress included orphan drugs as one of just three exclusions from the QSSD definition, evincing a clear intent to preserve Congress’ longstanding support and incentives for drugs treating small patient populations, namely populations of fewer than 200,000 patients.¹⁸

¹⁴ *Id.*

¹⁵ Orphan Drug Act of 1983, Pub. L. 97–414, §1(b), Jan. 4, 1983, 96 Stat. 2049.

¹⁶ The ODA defines the term “rare disease or condition” to mean “any disease or condition which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug.” See 21 U.S.C. § 360bb(a)(2).

“Rare Diseases at FDA,” Available at <https://www.fda.gov/patients/rare-diseases-fda> (Accessed April 7, 2023).

CMS's proposed approach to implementing Congress's exemption, however, fundamentally disrupts this purpose by leaving unprotected rare disease and rare cancer therapies that treat fewer than 200,000 patients even across multiple indications. When designating a drug as an orphan drug, FDA pays careful attention to the 200,000 patient prevalence limit. Further, FDA acknowledges that a drug may show promise even in multiple, different rare diseases. Such drugs may be eligible for multiple orphan designations because FDA considers the prevalence within each disease or condition.

By way of example, in 2014 the FDA approved AstraZeneca's LYNPARZA® (olaparib) as an oral orphan-designated monotherapy for patients with deleterious or suspected deleterious germline BRCA mutated (as detected by an FDA-approved test) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy.¹⁹ AstraZeneca has since continued to invest in advanced clinical research to refine and bring the clinical benefits of LYNPARZA to other patient populations: recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer (in 2017),²⁰ human epidermal growth factor receptor 2 (HER-2)-negative metastatic breast cancer (in 2018),²¹ gBRCAm metastatic pancreatic adenocarcinoma (in 2019),²² and somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) (in 2020).²³ Using the highest U.S. prevalence numbers available, the current total estimated disease prevalence across all four conditions is estimated to be less than 50,000 patients,²⁴ still far fewer than the 200,000 patient size contemplated by Congress in enacting the ODA. Yet, under CMS' proposed interpretation of the IRA's orphan drug exclusion, the 2018 approval of LYNPARZA for metastatic breast cancer likely would have resulted in the loss of the orphan drug exclusion for LYNPARZA from 2014 for advanced ovarian cancer, at a time when the therapy was approved for a small patient combined population.

LYNPARZA and other rare oncology products are often approved in late-stage treatment before data becomes available in front-line and adjuvant treatment trials. Furthermore, long-term follow-up on overall survivability can take five or more years and comes at significant cost. Moving forward, if a manufacturer knows further investment in an oncology product is running against a negotiation clock, companies may delay launch of or choose to not move forward in advancing research to learn whether a particular drug might also treat other conditions.

As is clear, CMS's approach will have the effect of including in the Negotiation Program orphan drugs treating patient populations well below the 200,000 threshold Congress sought to protect in the ODA, undermining the ODA's purpose and disturbing a carefully crafted framework

¹⁹ https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/206162lbl.pdf.

²⁰ https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208558s000lbl.pdf.

²¹ https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208558s001lbl.pdf.

²² https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208558Orig1s010lblrpl.pdf.

²³ https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208558s014lbl.pdf

²⁴ Analysis conducted based on disease prevalence numbers reported in the National Organization for Rare Disorders' Rare Disease Database (available at <https://rarediseases.org/rare-diseases>).

that has been remarkably successful in bringing new lifesaving treatments to patient populations that may otherwise have lacked access to any therapy for their rare condition.

In light of these significant concerns, we strongly urge CMS to exclude from negotiation any drug that, in aggregate, treats indications for which there are fewer than 200,000 patients.

- iii. *The 7- or 11-year period that must elapse before a drug or biological can be subject to negotiation should begin on the date a drug loses eligibility for the orphan drug exclusion.*

In the case of a drug that initially qualifies for the orphan drug exclusion from inclusion in a QSSD as outlined above, CMS should clarify that the 7- or 11-year period prior to negotiation eligibility begins to run only upon the loss of the orphan drug exclusion.

As discussed above, pursuant to section 1192(e) of the Act, a drug can only be classified as a QSSD (and hence be subject to negotiation) once “*at least 7 years...since the date of such approval [under section 505(c)]*” or “*at least 11 years...since the date of such licensure [under section 351(a)]*” have elapsed. This language must be read in the context of the orphan drug exclusion, which provides that: “[T]he term ‘qualifying single source drug’ does not include any of the following . . . [a] drug that is designated as a drug for only one rare disease or condition under section 526 of the [FDCA] and for which the only approved indication (or indications) is for such disease or condition.”²⁵

Under CMS’s guidance, a drug that initially qualifies for the orphan drug exclusion would lose this exclusion, and could potentially be classified as a QSSD, following the approval, with respect to the same active moiety, of a non-orphan indication or a new orphan indication for a distinct disease or condition. CMS’s guidance, however, does not address *when* such a drug could potentially be classified as a QSSD and hence becomes eligible for negotiation.

CMS should issue additional guidance to clarify that the 7- or 11-year pre-negotiation period would commence only upon the date a drug loses eligibility for the orphan drug exclusion. This outcome is supported by the statute’s plain language and scheme. Notably, the orphan drug exclusion constitutes a threshold exclusion from the definition of a QSSD.²⁶ It must follow from this structural placement that the 7- or 11-year pre-negotiation period that would otherwise apply to a QSSD is *tolled* until the first day after the orphan drug no longer meets the requirements of the orphan drug exclusion. Indeed, any other approach would defeat the intent of excluding relevant orphan drugs from the QSSD definition, including the statutory sub-elements. (Consider,

²⁵ See SSA § 1192(e)(3)(A).

²⁶ See SSA § 1192(e)(3)(A) (“Exclusions.—In this part, the term [QSSD] does not include any of the following...(A) Certain Orphan Drugs.”)

by contrast, the small-biotech exclusion, which was specifically inserted as an exclusion to the definition of a “*negotiation-eligible drug*” under section 1192(d)(2) of the Act.)²⁷

By issuing guidance that sets forth the interaction between the orphan drug exclusion and the QSSD definition in this way, CMS will be following the plain text of the statute. Additionally, we believe that CMS should interpret the Medicare Negotiation program in a way that supports and safeguards the important progress the ODA has achieved in sharing the benefits of medical innovation with patients with orphan diseases. The approach outlined here better enables innovator companies to pursue orphan indications by initiating the pre-negotiation period only upon a subsequent approval for a distinct disease or condition.

- iv. *CMS should carve out the original orphan drug exclusion-eligible indication when a product becomes QSSD eligible*

Under CMS’s guidance, a drug that initially qualifies for the orphan drug exclusion would lose this exclusion, and could potentially be classified as a QSSD, following the approval, with respect to the same active moiety, of a non-orphan indication or a new orphan indication for a distinct disease or condition. In the case of a drug that initially qualifies for the orphan drug exclusion from inclusion in a QSSD as outlined above, CMS should carve out the original approval(s) under the original orphan designation of the active moiety or active ingredient (and associated Total Expenditures) from the resulting QSSD which includes the subsequent or supplemental approvals of the active moiety or ingredient which do not qualify for the orphan drug exclusion.

As also above, pursuant to section 1192(e) “the term ‘qualifying single source drug’ does not include. . . [a] drug that is designated as a drug for only one rare disease or condition under section 526 of the [FDCA] and for which the only approved indication (or indications) is for such disease or condition.” By carving out the initial exclusion eligible use of the product, CMS can preserve the intent of Congress to protect the development of orphan drugs while maintaining the ability to negotiated expanded uses of the same active moiety or ingredient otherwise identified as a QSSD.

- D. CMS should clarify that it will consider only 12 months of claims data to assess the applicability of the low-spend Medicare drug exclusion from the QSSD definition, and should exclude beneficiary cost sharing from such calculation. (Section 30.1.2)

For IPAY 2026, CMS states that it will identify low-spend Medicare drugs with less than \$200,000,000 in combined Part B and D expenditures (inclusive of beneficiary cost sharing) and exclude them from the QSSD definition pursuant to section 1192(e)(3)(B) of the Act by considering PDE and Part B claims data for dates of service between June 1, 2022, and May 31,

²⁷ See SSA § 1192(d)(2) (stating that “term ‘negotiation-eligible drug’ shall not include... a qualifying single source drug that meets [the listed criteria]”).

2023. However, CMS states that “[t]o allow a reasonable amount of time” for Part D plan sponsors and Part B providers/suppliers to submit the necessary data, CMS will consider claims submitted by June 30, 2023.

AstraZeneca requests that CMS clarify that the additional 30-day period is merely a “grace period” for submission of claims with a date of service that falls within the 12-month timespan, and any claims with a date of service before or after that 12-month period, including those with a date of service that falls within the 30-day grace period, will not be considered for purposes of applying the low-spend Medicare drug exclusion. If, on the other hand, CMS were to cost data beyond 12 months, this could improperly reduce the number of drugs excluded as low-spend and accelerate a given drug’s inclusion in the Negotiation Program.

Furthermore, we request CMS reconsider its proposed policy of including beneficiary cost sharing in determining whether a prospective QSSD falls below the low-spend Medicare drug exclusion threshold of \$200,000,000. Because beneficiary cost sharing amounts are not costs paid by Medicare, these amounts should not be considered “total expenditures under Parts B and D” for the purposes of applying the low-spend Medicare drug exclusion.

- E. CMS should publicly disclose the methodology for calculating total expenditures and create a process to engage manufacturers to address potentially incorrect total expenditure data. (Section 30.2)

CMS states that it will identify “negotiation-eligible” Part D drugs for IPAY 2026 based on reviewing PDE data for the 12-month applicable period.²⁸ After calculating total expenditures for each drug, CMS will remove drugs that satisfy the exclusions provided in statute (e.g., small biotech drugs) and then identify the 50 QSSDs that have the highest total expenditures under Part D.²⁹ AstraZeneca supports this approach. CMS does not indicate that its calculations will be made public.

AstraZeneca supports the modified definition of “gross prescription drug costs” that CMS finalized as part of the CY 2024 Part C & D Policy and Technical rulemaking.³⁰ However, we urge CMS to publish (1) the rankings of negotiation-eligible drugs, (2) the total expenditures corresponding to each selected drug, and (3) the methodology the agency used to calculate total expenditures. CMS should also provide manufacturers of selected drugs with an opportunity to review and propose corrections to total expenditure data and/or methodological errors prior to the publication of this information. We believe that this transparent approach would improve the operation of the Negotiation Program by establishing accountability and transparency.

²⁸ Guidance at 12.

²⁹ *Id.*

³⁰ CY 2024 Policy and Technical Changes to the Medicare Advantage Program, Medicare Prescription Drug Benefit Program, Medicare Cost Plan Program, and Programs of All-Inclusive Care for the Elderly, Final Rule (88 Fed. Reg. 22,120 (April 12, 2023))

F. CMS takes a reasonable approach to ranking and selecting drugs based on Total Expenditures (Sections 30.2 & 30.3)

AstraZeneca supports the approach laid out in Section 30.2 for identifying the 50 qualifying drugs with the highest Total Expenditures under Part D of Title XVIII for QSSDs during the applicable 12-month period using Part D prescription drug event (PDE) data for each qualifying single source drug for dates of service beginning June 1, 2022, and ending May 31, 2023. As CMS clarifies in footnote n.3 of this initial guidance, Total Expenditures under Part D of Title XVIII are defined in section 1191(c)(5) as total gross covered prescription drug costs (as defined in section 1860D-15(b)(3)), and further defined in the Part D regulations at 42 CFR § 423.308 as amended in the CY 2024 Part C & D Policy and Technical Rule.³¹ This approach removes any ambiguity and applies Congressional intent in ranking negotiation-eligible drugs based on total gross drug spending in Medicare Part D.

CMS also clarifies in Section 30.3, after removing any biological products that qualify for delayed selection for biosimilar market entry, the agency will select the 10 highest-ranking negotiation-eligible drugs for negotiation in rank order. AstraZeneca supports this approach as it provides for the greatest amount of clarity and predictability for all stakeholders and complies with a clear reading of sections 1192(a) and 1192(b) of the statute.

II. Section 40: Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026

A. CMS should not limit the Medicare Drug Price Negotiation Agreement (the “Agreement”) to the Primary Manufacturer as the Primary Manufacturer may not always be in the best position to negotiate with CMS. (Section 40)

AstraZeneca strongly disagrees with CMS's rigid approach to determining with which manufacturer it will sign an Agreement. To the extent that one or more manufacturers meet the statutory definition of a “manufacturer” under the Negotiation Program, CMS states that it intends to enter into an Agreement only with the Primary Manufacturer of a selected drug, and the agency does not intend to enter into an Agreement with any Secondary Manufacturer. CMS intends to designate the entity that holds the NDA(s)/BLA(s) for the selected drug to be the Primary Manufacturer.

As discussed above, co-commercialization agreements are extremely common in the development and marketing of pharmaceutical products. AstraZeneca is concerned that CMS's approach would force manufacturers to potentially share with each other competitively sensitive information that they would not otherwise share pursuant to the terms of the co-commercialization agreement. This is because CMS's approach effectively requires the Primary Manufacturer—the holder of the NDA(s)/BLA(s)—to serve as the intermediary for information that might be pertinent

³¹ *Id.*

only to the secondary manufacturer. For example, the statute requires CMS to consider “current unit costs of production and distribution of the drug” and “market data and revenue and sales volume.” While the sharing of this information may not necessarily amount to an antitrust violation, it may represent competitively sensitive information that the parties would not otherwise share, even in their co-commercialization agreements. At a minimum, CMS should make available a process to allow Secondary Manufacturers to share information directly with CMS where: (a) the Primary Manufacturer is by statute, regulation or contract prohibited from sharing such information held by the Secondary Manufacturer; and/or (b) sharing of information by the Secondary Manufacturer to the Primary Manufacturer could have an anticompetitive effect.

In the absence of a process whereby CMS permits the submission of data from Secondary Manufacturers (and imposes some burden of compliance on the Secondary Manufacturer), CMS's approach would require manufacturers to revisit their co-commercialization arrangements and revise them to fit CMS's inflexible mold as much as possible. While CMS may believe that contracting with only one manufacturer is administratively simple, AstraZeneca believes that as CMS progresses through the negotiation process itself, it will become increasingly apparent that CMS will not be able to obtain all the necessary information from the holder of the NDA(s)/BLA(s) that is needed to effectively negotiate, particularly if CMS proceeds with aggregating different NDAs/BLAs into a single QSSD. For example, under CMS's overbroad approach to defining a QSSD, there could be multiple NDA/BLA holders and thus multiple Primary Manufacturers for any given QSSD.

CMS's approach would also unfairly expose the Primary Manufacturer to liability for violations to the Agreement perpetrated by the Secondary Manufacturer that are beyond the control of the Primary Manufacturer. Holding the Primary Manufacturer liable for non-compliance of a Secondary Manufacturer is not only unsupported by the statute, it is also an inefficient approach to ensuring compliance. AstraZeneca doubts that it will be administratively burdensome for CMS to require any relevant Secondary Manufacturer to sign what will effectively be a boilerplate Agreement, or at the very least, a shorter agreement that legally obligates the Secondary Manufacturer to comply with the statute's requirements and submit information directly to CMS. Even if there is some administrative burden, such burden is substantially outweighed by the benefits of an approach where CMS is able to independently and separately hold each manufacturer liable for their own non-compliance.

- B. CMS should permit the submission of data on a rolling basis and provide manufacturers with the opportunity to review information prior to publication to ensure that there is no competitively sensitive information disclosed. (Section 40.2)

CMS states that the Primary Manufacturer of a selected drug must submit data to inform the negotiation process by October 2, 2023.³² Data elements will include: information on the non-Federal average manufacturer price (non-FAMP) and any information that CMS requires to carry

³² Guidance at 27-28.

out negotiation, including the manufacturer-specific negotiation factors (e.g., research and development costs, prior federal financial support, data on pending and approved patent applications).³³ Given the vague and broad nature of these data elements, and the limited time to compile them, AstraZeneca requests that CMS consider using its enforcement discretion to allow manufacturers of selected drugs to submit these data on a rolling basis, as long as a more limited set of data are reported by the October 2 deadline.

Between the time that a manufacturer is formally made aware that their drug has been selected for negotiation on the selected drug publication date (September 1) and the deadline that CMS would impose for the submission of negotiation data (October 2), only 30 days will have elapsed. It will be extremely difficult for manufacturers to collect all of the necessary data within this 30-day period, especially if CMS proceeds with its approach of requiring only the “Primary Manufacturer” to submit all necessary information. Indeed, given that securing competitively sensitive information from Secondary Manufacturers may impact existing regulatory or contractual protections of specific data elements, complying with the 30-day timeline for information held by Secondary Manufacturers and others may be an impossibility.

CMS should permit manufacturers to submit additional information after the October 2 deadline on a rolling basis with a final submission deadline at a later date.

CMS should also provide advance notice to manufacturers of drugs likely to be included on the selected drug list prior to the September 1 selected drug publication date to allow adequate time for data collection. Advanced notice will also provide manufacturers with the opportunity to engage with CMS and collect data in a manner and format that will be most helpful to the agency and the negotiation process.

Finally, AstraZeneca is concerned that CMS intends to treat only certain elements of the submitted data as proprietary information, protected from disclosure under Exemption 4 of the Freedom of Information Act (FOIA) and only available for use by CMS and the Comptroller General.³⁴ At a minimum, CMS should provide manufacturers of selected drugs with the opportunity to review data in advance of publication, including the explanation for the MFP as required under section 1195(a)(2) of the Act, to ensure that no competitively sensitive information is disclosed to the public.

C. CMS should reconsider the breadth of the destruction of data requirements proposed for Primary Manufacturers and impose parallel data destruction requirements on itself. (Section 40.2.2.)

CMS intends to impose certain requirements on the Primary Manufacturer related to the use, disclosure, and destruction of data and other information received during the negotiation

³³ *Id.*

³⁴ *Id.* at 29.

process.³⁵ This includes a prohibition on the Primary Manufacturer conducting audio or video recording of any oral conversation between CMS and the Primary Manufacturer.³⁶ All information that the Primary Manufacturer receives during the negotiation period from CMS must also be destroyed within 30 days of a determination that the drug or biologic is no longer a selected drug.³⁷

AstraZeneca is concerned that CMS's imposition of a destruction of data requirement on manufacturers is overly broad and could undermine the smooth operation of the Negotiation Program. We anticipate that some manufacturers may be “repeat” selected drug manufacturers due to the nature of their drug portfolios and Medicare spending patterns. Indeed, the lack of any limit to the number of drugs subject to future negotiation (subject only to the Low-Spend Medicare Drug Exclusion) means that it is virtually inevitable that multiple drugs of a single manufacturer will be subject to selection and negotiation over time. In such situations, it would be in the interest of the Negotiation Program for that manufacturer to have access to past learnings and negotiation processes to enable their incorporation into business practices that support the manufacturer’s future participation in the Negotiation Program. As an example, Primary Manufacturers will need to develop detailed workflows and procedures for the processing of data for submission to CMS, and such processes should not be undone as a result of an overbroad data destruction policy.

At the very least, CMS should clarify that, when it notes “all information...receiv[ed] during the negotiation period from CMS shall be destroyed,” this excludes any work product produced by the Primary Manufacturer (as opposed to *received* from CMS) during the negotiation process.³⁸ For example, AstraZeneca does not believe that written notes of the process itself and relevant issues (e.g., why some R&D data is not acceptable/relevant) should be subject to destruction. Manufacturers should be able to maintain any manufacturer-created documents, including policies and procedures, as a matter of internal record, even if such documents are a reflection of learnings from the negotiation process.

If CMS moves forward with the overly broad data destruction policy proposed in the Guidance, AstraZeneca believes that CMS should hold itself to the same data-destruction requirements in the interest of public accountability and fairness. Nowhere in the Guidance does CMS discuss the agency's own use of the same information exchanged during the negotiation process, suggesting that CMS will be able to keep all information it receives and/or share such information as it pleases, including information *received* from a Primary Manufacturer, even after the selected drug status of the drug or biological product in question terminates. AstraZeneca does not believe that CMS should be able to retain such information in perpetuity, particularly while CMS imposes one-sided data destruction requirements on the Primary Manufacturer.

³⁵ Guidance at 30.

³⁶ *Id.*

³⁷ *Id.*

³⁸ *Id.*

D. CMS should establish a mechanism to allow dispensers access to the MFP at the point-of-sale, similar to the existing Part D Coverage Gap Discount Program. (Section 40.4)

CMS intends to require the Primary Manufacturer to ensure that entities that dispense drugs to MFP-eligible individuals, including pharmacies, mail order services, and other dispensers, have access to the MFP for the selected drug, meaning that the dispensing entity must pay no greater than the MFP for the selected drug.³⁹ CMS will allow Primary Manufacturers to comply with this requirement in one of two ways: (1) ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP (point-of-sale access); or (2) providing retrospective reimbursement for the difference between the entity's acquisition cost and the MFP within 14 days.⁴⁰ A Primary Manufacturer would be required to retain, for at least ten years from the date of sale, any records relating to sales of the selected drug to entities that dispense the selected drug to MFP-eligible individuals, including pharmacies, mail order services, and other dispensers for units of selected drug.⁴¹

We do not believe option (1) presents a practical method for providing the MFP to MFP-eligible individuals. As pharmaceutical products are not designated for a specific patient at the point of sale by a dispensing entity from the wholesaler or distributor, no mechanism currently exists in the supply chain to ensure that products purchased at MFP would be dispensed to an MFP-eligible individual. Further, most drug purchases by dispensing entities are from wholesalers and specialty distributors; accordingly, effectuating a patient-based purchasing price model would depend on the cooperation of wholesalers and specialty distributors themselves, who are not held directly liable for non-compliance with the requirement to offer the MFP. Additionally, AstraZeneca believes that these types of models would lead to significant diversion of drugs purchased at MFP to non-MFP eligible patients.

In addition, while we support the concept of providing retrospective reimbursement to effectuate the MFP, existing retrospective reimbursement mechanisms are not designed to provide payment from a manufacturer directly to a dispensing entity, nor do current systems support a payment window as short as 14 days. Rather, these payments are made (after a minimum of 30 days) to large Group Purchasing Organizations or Pharmacy Benefit Managers, who are then responsible for the pass-through of those discounts to their member entities. Existing models also would not presently ensure that MFP-related retrospective reimbursements would be passed through to the dispensing entity itself. Existing infrastructure does not support the exchange of dispensing data from the pharmacy to the manufacturer, nor do manufacturers store payment data for each individual pharmacy to allow for direct reimbursement. Any such exchange of data would almost certainly exceed a 14-day period of time and therefore render CMS's approach operationally unfeasible.

³⁹ *Id.* at 31-32.

⁴⁰ *Id.* at 32.

⁴¹ *Id.*

AstraZeneca therefore supports the industry’s recommended approach, as outlined by PhRMA and BIO, to implement the MFP along the lines of the current Part D Coverage Gap Discount Program (CGDP), which facilitates manufacturer price concessions at the point-of-sale (POS) for Part D beneficiaries. Under the current CGDP, CMS relies on a third-party administrator (TPA) to aggregate Part D data, distribute invoices to manufacturers, reconcile disputes, and reimburse Part D plans for “advancing” access to the manufacturer discount at the point-of-sale. This current process could easily accommodate access to the MFP at the point-of-sale, ensuring that dispensers receive the full benefit of the MFP at the time of dispensing of an MFP-eligible drug, rather than relying on a lengthy reimbursement methodology. CMS could also impose requirements on Part D sponsors to validate that a drug is a selected drug offered to an MFP-eligible individual, and to ensure there are no multiple discounts (e.g., 340B discounts, discounts provided under the new Manufacturer Discount Program).

AstraZeneca also opposes CMS’s requirement that the Primary Manufacturer retain for at least ten years from the date of sale any records relating to sales of the selected drug to entities that dispense the selected drug to MFP-eligible individuals. Maintaining such detailed data for ten years is extraordinarily burdensome and costly. AstraZeneca recommends that CMS reduce the required timeframe to 6 years, consistent with the statute of limitations for the False Claims Act⁴².

- E. CMS should separately require the Secondary Manufacturer of any selected drug to make the MFP available to MFP-eligible individuals and entities rather than hold the Primary Manufacturer responsible for behavior beyond their control. (Section 40.4)

CMS states that Primary Manufacturers would be responsible for ensuring that the MFP is made available to pharmacies, mail order services, and other dispensers that dispense the selected drug to MFP-eligible individuals, including to ensure that the MFP is available for units of the selected drug for which there is a Secondary Manufacturer.⁴³

As stated above, we do not believe it is appropriate for CMS to hold Primary Manufacturers liable for any and all violations of Secondary Manufacturers with respect to making the MFP accessible to eligible entities. We further do not see any impediment to CMS directly binding Secondary Manufacturers to these same requirements via separate agreements, particularly if CMS adopts such a broad approach to defining a QSSD under which the manufacturer marketing a particular product may or may not be the Primary Manufacturer. The statute does not distinguish between “Primary” and “Secondary” manufacturers, and while CMS may believe this distinction contributes to administrative simplicity, as soon as legal obligations and consequences (e.g., civil monetary penalties) attach to the agency’s administrative decisions, such decisions must be supported by the statute. Absent clear statutory authorization, CMS cannot impose legal liability on one manufacturer for the violations of a different manufacturer; the agency must directly impose the consequences of any violation on the violating entity.

⁴² 31 U.S.C. § 3731(b)(1).

⁴³ Guidance at 32.

III. Section 50: Negotiation Factors

AstraZeneca supports CMS's solicitation of information from patients and Medicare beneficiaries to inform the negotiation process and urges CMS to give substantial weight to the patient voice. We further support CMS's policy of not considering quality-adjusted life years (QALYs) for purposes of the Negotiation Program and the agency's close scrutiny of any comparative effectiveness research that may rely on QALYs for its conclusions. However, we urge CMS to allow for manufacturer input regarding the selection of therapeutic alternatives, and to develop a more detailed framework for how the agency will consider therapeutic alternatives and comparative effectiveness data based on five core principles.

A. AstraZeneca supports CMS's solicitation of information from patients and Medicare beneficiaries and urges CMS to give substantial weight to the patient voice (Section 50.2).

As described in the Guidance, CMS will consider therapeutic alternative and comparative effectiveness data submitted by Medicare beneficiaries, academic experts, clinicians, and other interested members of the public.¹⁹ We strongly support this solicitation, and we note the patient voice is often ignored, even in the comparative effectiveness research that purports to assess the best treatments for patients. This is particularly true for minority and underserved people living with rare diseases, who face additional disparities in access to care, including differences in health care utilization, delayed or missed care due to a lack of transportation or work flexibility, and a lack of representation in clinical trials and research. AstraZeneca therefore urges CMS to give substantial weight to the patient experience in CMS's evaluation of therapeutic alternatives and comparative effectiveness. Factors such as patient convenience due to route of administration, caregiver burden, and improvements in quality of life not otherwise measured by endpoints in a clinical trial nevertheless represent a significant benefit to the patient experience. Such a seemingly innocuous benefit can directly impact other health outcome metrics, such as medication adherence and patient self-sufficiency, through an improved ability to consistently engage in gainful employment. We urge CMS to not only take into account the beneficiary and caregiver experience, but to prioritize it when evaluating the value of a drug product.

B. CMS should develop a more detailed framework for how the agency will consider therapeutic alternative and comparative effectiveness data based on five core principles (Section 50.2)

As described in the Guidance, CMS will consider therapeutic alternative and comparative effectiveness data submitted by Medicare beneficiaries, academic experts, clinicians, and other interested members of the public.²¹ Improved clinical outcomes for patients should be a shared objective between CMS and pharmaceutical manufacturers and multifaceted consideration of a selected drug's clinical value should be the basis of any evaluation. AstraZeneca supports a framework for assessment of clinical value that considers the following five core principles:

1. The process of clinical value assessment should be transparent. Using scientific principles, consistent methodology, and appropriate evidence, various stakeholders should be able to come to similar conclusions.

2. While adhering to consistent methodology, clinical value assessments should consider contextual factors associated with the disease in question. This is particularly important for diseases associated with high unmet need. Aside from the obvious recruitment challenges in rare disease clinical trials, the basic pathophysiology of many rare diseases is less well understood compared to more common diseases. Because of this, clinical trials for rare disease treatments may be non-comparative and often use endpoints that are not specifically developed to capture the full impact of the rare disease or its treatment. Further, cancer is not one disease but rather a cohort of related diseases that requires a range of treatments with different goals and outcomes that can vary over the course of the disease. Relevant trial endpoints therefore also vary according to cancer type (e.g., solid or blood cancers) and staging (I-IV), intent of treatment (e.g., curative vs. palliative) and feasibility, which is the likelihood of capturing relevant endpoint data (e.g., tumor growth and spread, quality of life assessments from people with cancer) within time and cost constraints.

It's also important to consider whether a drug was approved for a disease when there was no available or adequate therapy available, recognize progress against hard-to-treat illnesses, curative potential, impact to public health, and the impact of a product on health disparities and improved outcomes for underserved or historically marginalized groups.

3. Appropriate therapeutic alternatives must be assessed, based on clinical, not economic factors. Therapeutic alternatives should be licensed and approved for the disease in question and there should be sufficient data to make a valid assessment of each alternative's clinical value feasible. For many rare diseases with existing treatments, there may be only one appropriate therapeutic choice. And, as noted above, the manufacturer should have input regarding the identification of therapeutic alternatives.

4. The perspective of clinical value assessment should be multifaceted and inclusive of factors related to health equity. The assessment must include not just short-term efficacy endpoints used in clinical trials, but safety, long-term health outcomes, patient experience factors such as route and frequency of administration, impacts on population health equity, health system resource use, and societal impacts outside the healthcare system as well. A study conducted by the EveryLife Foundation²³ concluded that 55 percent of the total burden of rare diseases is experienced outside of the healthcare system. Importantly, these impacts are still very much part of the lived experience of rare disease patients.

In assessment of cancer treatment effect, particularly for early-stage cancer, consideration should be given to oncology-relevant endpoints other than overall survival (OS) which have intrinsic value for decision-making. In early-stage cancer OS data takes time to mature or may not be possible to collect in the longer term. Indication, intent of treatment, and feasibility of measuring patient-relevant outcomes (e.g., disease-free survival, relapse-free survival, delay or avoidance of

subsequent treatments, QoL) within a reasonable timeframe should be evaluated when considering oncology-relevant endpoints in value assessments to allow patients to benefit from innovative treatments.

Health equity deserves additional consideration. The Centers for Disease Control and Prevention defines health equity as, “the state in which everyone has a fair and just opportunity to attain their highest level of health.” Equity of access for cancer patients is vital, as the benefits are only seen if people with cancer are aware of treatment options, and able to access and adhere to treatment. A study in the *Journal of the American Medical Association* found in disadvantaged neighborhoods, a lack of physicians and healthcare resources, weak referral systems, poor social support networks, and barriers to travel for initial and ongoing care negatively impact outcomes for people with cancer.⁴⁴ Access to treatment options for these patients may address a disproportionately higher unmet medical need. Drugs targeting chronic conditions may present additional benefits to undertreated populations or minority groups disproportionately impacted by disease. For example, two recent clinical trials with sodium glucose co-transporter-2 (SGLT2) inhibitors, demonstrated a reduction in heart failure (HF) hospitalization or cardiovascular mortality risk in patients with HF and reduced ejection fraction (HFrEF) and signaled a potentially greater effect in Black and Asian patients randomized to treatment compared to other groups.⁴⁵ Health equity is also important in chronic diseases, such as COPD, where socioeconomic, occupational, and environmental factors, as well as access to healthcare, impacts prevalence and outcomes in different patient groups.⁴⁶

5. Data used to inform a clinical value assessment will need to come from a wide variety of sources. Appropriate data sources should include, but should not be limited to, clinical trials, patient registries, and other real-world data. Patient registries and other real-world data have been important sources of data to demonstrate the certain kinds of treatments that are hard to evaluate in clinical settings. Real-world data is also needed to assess some endpoints not easily measured in clinical trial settings, such as caregiver burden and non-medical costs. Data collected from patients via patient-reported outcomes (PROs) including quality of life, should be routinely and consistently incorporated into value assessments, along with the value components that are already used relating to safety and efficacy.

Finally, CMS should consider setting the MFP for selected drugs at the ceiling price for those products that meet the FDA’s definition of unmet need, evaluated across a product’s lifecycle; and products that represent a significant therapeutic advance. CMS’s definition of “unmet need” is narrower than the FDA definition and may dampen industry interest in the post-

⁴⁴ Cheng E, Soulos PR, Irwin ML, et al. Neighborhood and Individual Socioeconomic Disadvantage and Survival Among Patients with Nonmetastatic Common Cancers + Supplemental content. *JAMA Netw Open*. 2021;.

⁴⁵ Morris AA *et al*, Sodium-Glucose Cotransporter-2 Inhibitors in Heart Failure: Racial Differences and a Potential for Reducing Disparities. *Circulation*, 2021.

⁴⁶ [Pleasant RA, Riley IL, Mannino DM. Defining and targeting health disparities in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2016

approval research that often leads to additional indications for conditions or sub-populations with significant unmet need. Further, CMS could leverage the existing New Technology Add-On Pathway (NTAP) definition for “substantial clinical improvement” which provides the agency with an established measure for evaluating the value of certain products.

- C. AstraZeneca supports CMS’s policy of not considering QALYs in applying comparative effectiveness research, and urges CMS to give substantial weight to the patient voice and experience in its assessment of a selected drug’s comparative effectiveness. (Section 50.2)

As required by statute, CMS will assess a selected drug’s comparative effectiveness as compared to “therapeutic alternatives.”⁴⁷ In so doing, CMS stated the agency will not use evidence from comparative clinical effectiveness research that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill, including quality-adjusted life years (QALYs).⁴⁸ To the extent studies regarding comparative effectiveness employ QALYs in its analysis, CMS will not consider it unless it is able to separate such evidence.⁴⁹ AstraZeneca supports CMS’s policy of not considering QALYs for purposes of the Negotiation Process, which is consistent with the plain statutory language of the IRA. We similarly support the agency’s scrutiny of any comparative effectiveness research that may rely on QALYs for its conclusions.

- D. CMS should allow for manufacturer input on the selection of therapeutic alternatives and on the development of a more detailed framework for how the agency will identify therapeutic alternatives and evaluate comparative effectiveness. (Section 50.2)

AstraZeneca further urges CMS to allow for manufacturer input into the selection of therapeutic alternatives in applying comparative effectiveness research as part of the Negotiation Program. In the Guidance, CMS outlines a flexible approach to considering therapeutic alternatives and evaluating comparative effectiveness. We note that AstraZeneca has serious concerns that certain studies have drawn improper comparisons across therapies (e.g., comparing targeted novel treatment to chemotherapy, etc.). As a result, we have a number of open questions including, for example: Will CMS consider products that treat the same disease area, or that treat the same specific indication, as therapeutic alternatives? How will CMS distinguish between different mechanisms of action or routes of administration, even when the drugs under consideration treat the same disease area or specific indication? How will CMS consider comparative effectiveness research in light of demonstrable differences in heterogeneous patient populations where what may work for one patient may not work for another, thereby confounding the comparability of comparative effectiveness comparisons? How does CMS intend to resolve conflicting evidence as it relates to a selected drug’s comparative effectiveness?

⁴⁷ *Id.* at 36.

⁴⁸ *Id.*

⁴⁹ *Id.*

Given these significant uncertainties, at a minimum, AstraZeneca urges CMS to provide manufacturers with an opportunity to engage with CMS and review CMS's methodology for the selection of therapeutic alternatives, before CMS makes such a determination. We also urge CMS to consider only on-label indications in selecting therapeutic alternatives, as off-label indications have not been approved by FDA and have significantly less robust data regarding safety and efficacy, relative to on-label uses.

IV. Section 60: Negotiation Process

A. CMS should consider a selected drug's multi-faceted clinical value, rather than narrowly focusing on R&D spend and recoupment.

As described in Section 60 of the Guidance, CMS is proposing a four-step process to determine an initial offer and counteroffer for a selected drug. Specifically, CMS intends to: (1) identify indications for the selected drug and therapeutic alternative(s); (2) use as a starting point the Part D net price for Part D drug therapeutic alternative(s) and/or Part B average sales price for Part B therapeutic alternative(s); (3) evaluate clinical benefits of the selected drug to adjust the starting point; and (4) further adjust the preliminary price through consideration of manufacturer-specific data (e.g., R&D costs; current unit costs of production and distribution) to determine the initial offer price. While AstraZeneca supports CMS's proposal to prioritize the consideration of clinical benefits, we are concerned that CMS may be putting undue weight on certain manufacturer-specific factors.

AstraZeneca appreciates that CMS is required by statute to take into consideration certain factors—including R&D costs—in setting the maximum fair price (MFP) for a selected drug. However, such factors are to be considered only “as applicable to the drug” and not all of the statutory negotiation factors must be weighted equally. The manufacturer-specific factors—including R&D costs—are difficult to categorize, and decoupling specific costs for assets does not represent the full cost or value of a given drug. Overreliance on these factors could thus result in an arbitrary pricing methodology.

As also noted in our comments regarding Section 60.3.4 of the Guidance, AstraZeneca urges CMS to instead prioritize the clinical statutory negotiation factors. Specifically, CMS should focus on whether a selected drug demonstrates a clinical benefit and addresses an unmet need in calculating the MFP. This approach would best preserve incentives for innovation, establish a clear and predictable methodology for determining drug pricing, and enable CMS to meet its statutory obligations under the IRA.

B. CMS should allow for manufacturer input on the selection of therapeutic alternatives for purposes of identifying the “starting point” for the initial MFP offer calculation.

As described above, CMS is proposing a four-step process to determine an initial offer and counteroffer for a selected drug. While AstraZeneca broadly agrees with this framework, we have some concerns regarding how it might be implemented.

For instance, as to this first step, as described in response to our comments to Section 50.2, above, manufacturers should be given an opportunity to weigh in regarding CMS's selection of therapeutic alternatives as certain studies have drawn improper comparisons across therapies. In addition, an off-label product is priced for use in its licensed indication, making its price an unsuitable starting point for negotiations.

C. CMS should provide a clearer framework for the directional adjustments it would make when evaluating clinical benefit relative to therapeutic alternatives. (Section 60.3.3.1)

After identification of therapeutic alternatives for purposes of establishing a starting point for negotiations, CMS intends to adjust the starting point based on the clinical benefit that the selected drug confers as compared to its therapeutic alternatives. CMS will broadly evaluate the body of clinical evidence through a CMS-led literature review, and CMS may also analyze Medicare claims data or other pharmaceutical drug datasets for utilization patterns, clinical data, or other information relevant to the selected drug and its therapeutic alternatives. CMS's adjustments to the starting point will be referred to as the "preliminary price."

While AstraZeneca appreciates that CMS is establishing a flexible methodology for adjusting a selected drug's starting point based on clinical benefit, we believe CMS should provide clearer guidance on both specific elements that will be evaluated, the weight applied to any one individual element, and the directional adjustments CMS would make based on its evaluation of such elements and their relative weight. For example, how will CMS weigh the fact that the selected drug in question was the *first* in class among all therapeutic alternatives? This type of innovation should invariably result in an upward adjustment to the starting point (if the starting point is below the statutory ceiling). In short, CMS should provide a framework that clearly indicates what factors and qualitative evidence could result in a selected product achieving a preliminary price at or near the ceiling price and/or an initial offer at or near the relevant ceiling price.

In addition, we recommend if a selected drug's statutory ceiling price is the net price (vs a percentage of non-FAMP), then the MFP should be set at the ceiling price (the net price) for the selected drug. This approach is appropriate because brand-to-brand competition has already resulted in substantial price reductions. This approach is operationally feasible as CMS has access to the necessary price data to determine the ceiling price based on net price.

D. CMS should apply special considerations when evaluating selected drugs, such as orphan drugs due to their unique circumstances. (Sections 60.3.3.2)

AstraZeneca appreciates CMS’s thoughtful approach and analytical framework for adjusting the starting point of a selected drug without therapeutic alternatives based on unmet need. CMS intends to adjust the starting point based on whether the selected drug fulfills an unmet medical need, a determination that will be made based on the “totality of relevant information and evidence submitted and gathered through the agency's analysis . . .”⁵⁰

However, as a leader in rare disease and rare cancer treatment development, we are deeply interested that CMS’s clinical benefit assessment for selected drugs without therapeutic alternatives is appropriately calibrated to account for the unique characteristics of rare disease. We appreciate that CMS has, elsewhere in the Guidance, recognized the need to work with stakeholders to “support orphan drug development.”⁵¹

As recommended above, CMS should begin at the statutory ceiling price for any selected drugs for which there are no therapeutic alternatives—which would include many rare disease therapies—rather than the FSS or “Big Four Agency” pricing. This would recognize the inherent value of a therapy that addresses an unmet need.

Additionally, regardless of whether it identifies therapeutic alternatives, CMS should apply upward adjustments for drugs with orphan indications, drugs that represent a significant therapeutic advance, and drug which addressed unmet need(s). In particular, determination of unmet medical need must explicitly include a framework for weighing the patient and caregiver voice, in addition to clinical factors.

- E. Manufacturer-specific factors should not be used, or should have a limited impact on pricing, for drugs that represent a therapeutic advance or address an unmet need (Section 60.3.4).

As to the fourth step in the process, AstraZeneca urges CMS to prioritize the clinical negotiation factors. Specifically, CMS should focus on whether a selected drug demonstrates a clinical benefit and addresses an unmet need in calculating the MFP. Under these circumstances, CMS should apply little to no weight to the manufacturer-specific factors. This approach would best preserve incentives for innovation, establish a clear and predictable methodology for determining drug pricing, and enable CMS to meet statutory obligations of the IRA.

V. Section 70: Removal from Selected Drug List Before or During Negotiation, or After an MFP is in Effect

- A. CMS should establish a grace period to account for situations where a generic/biosimilar is approved prior to the end of the negotiation period but marketed shortly after the negotiation period ends.

⁵⁰ *Id.* at 52.

⁵¹ *Id.* at 11.

Under section 1192(c) of the Act, a selected drug will no longer be subject to the negotiation process if FDA has approved a generic drug or licensed a biosimilar product that identifies the selected drugs as its reference product and CMS determines that the generic drug or biosimilar product is marketed pursuant to such approval or licensure. CMS will consider an approved generic drug or licensed biosimilar biological product to be marketed when the PDE data reveals that the manufacturer of the generic drug or biosimilar biological product has engaged in bona fide marketing of that drug or product.⁵² If CMS makes a determination regarding generic drug or biosimilar biological product market availability on or after the selected drug publication date, and before or during the negotiation period for an initial price applicability year, the selected drug will not be subject to the negotiation process for the negotiation period, and an MFP will not be established.⁵³

AstraZeneca urges CMS to establish a “grace period” when a generic/biosimilar to a selected drug receives FDA approval/licensure before the end of the negotiation period. Specifically, CMS should consider marketing data for a specified period *after* the negotiation period ends (e.g., 30 days) to determine whether a generic/biosimilar is in fact being marketed. As some generic/biosimilar manufacturers may encounter unexpected challenges during the marketing ramp-up period, we believe it is appropriate for CMS to exercise some flexibility to consider this marketing data so long as the product was approved/licensed *before* the conclusion of the negotiation period. Allowing this grace period will enable the biosimilar to better compete once it actually enters the market without having the reference product subject to an MFP.

The generic/biosimilar manufacturer would have the burden of submitting such data to CMS. For instance, in the case of IPAY 2026, CMS would consider marketing data between August 1, 2024, and September 1, 2024 so long as the generic/biosimilar is approved/licensed prior to August 1.

CMS should also consider an interpretation of the law that allows a reference product to exit the Program if a generic or biosimilar product is marketed after the “negotiation period” but before the IPAY begins. Such reading aligns with the statutory definition of a “qualifying single source drug” (QSSD)—a threshold requirement for a drug to be subject to price setting. The statute defines a QSSD “with respect to an initial price applicability year,” indicating that a product’s status as a QSSD should still exist as of the first day of the IPAY. Thus, a product that has become multisource before the IPAY should not be subjected to price setting. This approach would ultimately preserve market incentives for generic/biosimilar resources and avoid spending agency time/resources negotiating a product which will have meaningful generic/biosimilar competition before an IPAY begins.

VI. Section 80: MFP Eligible Individuals

⁵² *Id.* at 62.

⁵³ *Id.*

- A. CMS should clarify that the term “MFP eligible individual” excludes an individual receiving services in a Part A hospital stay. (Section 80)

CMS states that in the case of a selected drug that is furnished to an individual enrolled under Medicare Part B (including an individual enrolled in an MA Plan) by a hospital, physician or other provider, the individual must be provided access to the MFP “*if payment may be made under Part B for such selected drug.*”⁵⁴ This mirrors the underlying statutory definition of an MFP eligible individual, which with respect to a selected drug:

*in the case such drug is furnished or administered to the individual by a hospital, physician, or other provider of services or supplier, an individual who is enrolled under part B of title XVIII, including an individual who is enrolled in an MA plan under part C of such title, if payment may be made under part B for such selected drug.*⁵⁵

AstraZeneca requests that CMS clarify that manufacturers are not obligated to provide access to the MFP for a Medicare patient in a Part A stay. Notably, the statute makes no reference to Medicare Part A. In addition, while the statute requires only that “payment may be made under Part B,” this does not loop in Part A utilization, which is administered in the inpatient setting and therefore not eligible for payment under Part B. This language is instead a clear reference to Medicare Advantage utilization, which involves payment under Part C for a drug that would otherwise be paid for under Part B. While we believe this position is supported by the plain text of the statute, we would appreciate CMS explicitly confirming our understanding to avoid the diversion of MFP-purchased drugs beyond the statutory scope of the Negotiation Program.

VII. Section 90: Manufacturer Compliance and Oversight

- A. CMS should issue guidance to assist manufacturers with compliance and establish an enforcement policy to prevent diversion and duplicate discounts. (Section 90.2)

During a price applicability period, a Primary Manufacturer must provide MFP-eligible individuals with access to the MFP for a selected drug at the pharmacy, mail-order service, or other dispenser at the point-of-sale.⁵⁶ Additionally, the Primary Manufacturer must provide the pharmacy, mail-order service, or other dispenser with access to the MFP for the selected drug. In the Guidance, CMS proposes that Primary Manufacturers must establish safeguards to ensure that MFP-eligible individuals, pharmacies, mail-order services, and other dispensers can access the MFP on units of the selected drug for which there are Secondary Manufacturers.⁵⁷ CMS also

⁵⁴ *Id.* at 63 (emphasis added).

⁵⁵ SSA, § 1191(c)(2)(B).

⁵⁶ Guidance at 64.

⁵⁷ *Id.*

proposes to establish procedures for reporting violations related to MFP access for MFP-eligible individuals enrolled in PDPs or MA-PDs.⁵⁸

AstraZeneca is concerned that CMS's proposed approach puts responsibility on the Primary Manufacturer for activity well beyond its control and does not address the possibility of diversion. As discussed above in section II.A of our comments, we do not see any administrative challenges with CMS separately requiring Secondary Manufacturers to sign near-identical agreements that directly obligate them to comply with the various requirements relating to the Negotiation Program that are directly under their control, including but not limited to, ensuring access to the MFP for selected drugs that they distribute to, or on behalf of, MFP-eligible individuals. Relatedly, we do not believe that Primary Manufacturers should face potential liability for the pharmacy or provider failing to provide the MFP to MFP-eligible individuals.

AstraZeneca additionally requests that CMS issue guidance to assist manufacturers with compliance (e.g., by outlining verification measures manufacturers may employ to confirm that a particular selected drug was in fact dispensed to an MFP-eligible individual, and to confirm that the drug was not subject to a 340B duplicate discount). CMS should also establish (i) an enforcement policy to take action against the diversion of selected drugs purchased at MFP by dispensing entities, and (ii) a dispute resolution process to adjudicate disputes regarding 340B duplicate discounts, in addition to a patient's or dispensing entity's claim to MFP pricing.

B. CMS's proposed requirement that there must be “robust and meaningful” competition by the generic/biosimilar to exclude the branded drug from being a QSSD is not supported by statute. (Section 90.4)

CMS states that, if it identifies a generic or biosimilar to a selected drug, the agency will additionally require that “robust and meaningful competition exists in the market” prior to concluding that the drug no longer qualifies as a QSSD subject to the Negotiation Program. CMS intends to make this determination based on the monitoring of PDE data and may “include whether the generic drug or biosimilar biological product is regularly and consistently available for purchase through the pharmaceutical supply chain, and whether it is available for purchase by community retail pharmacies in sufficient quantities from their wholesale suppliers.”⁵⁹

In adopting this policy, CMS relies on sections 1192(e)(1)(A)(iii) and 1192(e)(1)(B)(iii) of the Act for drug products and biological products, respectively.⁶⁰ While these provisions require that a generic or biosimilar be “marketed” in order for the branded product to lose its QSSD status, the term “marketed” is best understood consistent with its ordinary meaning, which is to “expose

⁵⁸ *Id.*

⁵⁹ *Id.* at 68.

⁶⁰ *Id.* 67-68.

for sale in a market”⁶¹ or “to offer products for sale to buyers.”⁶² Nothing about the “ordinary meaning” of the term “marketed” suggests that sellers must sell the product in a “robust and meaningful” manner.⁶³ CMS should not operate beyond the statute by establishing a separate “robust and meaningful competition” standard. The availability of the generic/biosimilar for purchase should be sufficient to make a determination that the product is “marketed” as required by the statute. At the very least, a single sale of the generic/biosimilar product should suffice.

To our knowledge, CMS does not apply a “robust and meaningful” standard to any other aspect of its administration of the Medicare program. There are many issues that could arise in the exercise of such a standard for which CMS cannot adequately account. We are concerned that this standard is too vague for CMS to implement in a non-arbitrary manner, and it deprives manufacturers of regulatory predictability regarding the treatment of their products under the Medicare program.

VIII. Section 100: Civil Monetary Penalties

- A. CMS should provide manufacturers with an opportunity to cure potential deficiencies in providing access to the MFP, in addition to generally providing more transparency regarding its enforcement policies.

CMS will impose civil monetary penalties (CMPs) on a Primary Manufacturer of a selected drug that enters into an Agreement but does not provide access to a price less than or equal to the MFP for MFP-eligible individuals, pharmacies, mail-order services, other dispensers, hospitals, physicians, or other providers or suppliers.⁶⁴ CMPs may also be levied for the provision of false information as it relates to various aspects of the Negotiation Program.⁶⁵

AstraZeneca requests that CMS provide an opportunity for manufacturers to cure any suspected deficiencies identified by CMS prior to the imposition of CMPs. Moreover, we request that CMS provide more transparency regarding how it intends to assess and track potential violations. Specifically, CMS should create a mechanism for notification and engagement around potential concerns about the provision of MFP to MFP-eligible individuals and entities,

⁶¹ Definition of “Marketed”, Merriam-Webster Online Dictionary (last accessed March 25, 2023), <https://www.merriam-webster.com/dictionary/marketed>.

⁶² Definition of “Marketed”, Cambridge Dictionary Online (last accessed March 25, 2023), <https://dictionary.cambridge.org/us/dictionary/english/market?q=marketed>.

⁶³ Indeed, in other contexts in the Medicare program, CMS has interpreted the term “marketing” to simply be the date a technology becomes available on the U.S. market. *See* 79 Fed. Reg. 49854, 49931 (Aug. 22, 2014). For example, under the New Technology Add-on Payment Program, CMS can look to the market entry date of a new technology to determine the time period for which this additional payment applies. Consistently, the agency has rejected arguments from applicants related to low volume following FDA approval, stating in part, “we do not believe that case volume is a relevant consideration for making the determination as to whether a product is “new.”” *See* 82 Fed. Reg. 37990, 38111 (Aug. 14, 2017).

⁶⁴ Guidance at 68.

⁶⁵ *Id.* at 70.

compliance with the Negotiation Agreement, and/or concerns about the veracity of manufacturer-submitted information.

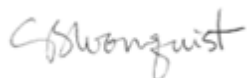
IX. Section 110: Part D Formulary Inclusion of Selected Drugs

Within the guidance CMS restates the statutory requirement that any drug selected for negotiation, with an MFP in effect, must be covered on all Part D formularies. We believe CMS should consider additional steps to ensure that patient access to a selected drug remains in place after the product is negotiated. The entrance of negotiated products into the Part D market will undoubtedly impact payer incentives and their approach to formulary and benefit design. Therefore CMS should institute guardrails and monitoring to ensure patients retain access to negotiated products and robust formulary designs capable of providing options which continue to meet patients' needs. In particular, we recommend that CMS closely monitor plans' tiering decisions, cost-sharing levels, and patient OOP exposure for both drugs subject to an MFP and potential class alternatives in order to evaluate impacts on the quality of benefits and access.

X. Conclusion

AstraZeneca thanks you for the opportunity to submit comment regarding the Guidance and look forward to continuing to engage with CMS as it implements the Negotiation Program for IPAY2026 and beyond. I can be reached at 202-350-5542 or christine.bloomquist@astrazeneca.com with any questions.

Sincerely,



Christie Bloomquist
Vice President, US Corporate & Government Affairs

April 14, 2023

Centers for Medicare and
Medicaid Services
7500 Security Blvd.
Baltimore, MD 21244

Submitted electronically

RE: Initial guidance on the Medicare Drug Price Negotiation Program

Dear Administrator Brooks-LaSure and Deputy Administrator Seshamani:

ATI Advisory is pleased to submit comments on CMS' initial guidance regarding implementation of the Medicare Drug Price Negotiation Program for Initial Price Applicability Year 2026.

The Medicare negotiation provision of the Inflation Reduction Act promises to save approximately \$100 billion over the next ten years. CMS' comprehensive and detailed initial guidance represents the critical first step towards successful implementation of this new program. We offer the following comments, which respond broadly to several topics covered in CMS' initial guidance, including:

- Handling of new NDAs/BLAs
- Managing information submitted by manufacturers
- Managing and evaluating data on therapeutic alternatives
- Developing price offers
- Monitoring bona fide marketing
- Guiding Part D formulary management of selected drugs

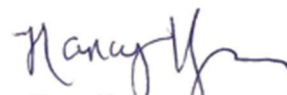
We appreciate your consideration of our input.

Sincerely,



Anna Kaltenboeck

Head



Nancy Yu

Senior Advisor

Prescription Drug Reimbursement Practice
ATI Advisory

Section 30. Identification of Selected Drugs for Initial Price Applicability Year 2026

Although CMS is not accepting comments on Section 30, we applaud the decision to determine whether a drug is a Qualifying Single Source Drug (QSSD) based on the first NDA or BLA for its active moiety or active ingredient. The alternative, to treat each NDA or BLA as a separate entity, would effectively result in the availability of substitute products that are not subject to the MFP. Because this would allow manufacturers to shift patients to a substitute product, savings to Medicare and its beneficiaries would be limited. CMS' approach appears to be consistent with assumptions made by the Congressional Budget Office (CBO) in its estimate of savings of nearly \$100 billion over the next 10 years.¹ It also provides clarity and predictability to market participants, including manufacturers, Part D plans, and providers.

Section 30.1.3. Plasma-Derived Product Exclusion from Qualifying Single Source Drugs

We also support CMS' interpretation of the exclusion from negotiation of plasma-derived products, such as immunoglobulins and clotting factors, and note that this exclusion should not extend to other products that utilize human tissue, such as cell and gene therapies. Blood products have different economics from other prescription drugs and treatments because they rely on the harvesting of blood from donors. This makes them uniquely sensitive to variable costs and uncertainties in supply, such as infectious disease.² The cost of producing other prescription products is more stable and predictable, as well as generally lower, than those of plasma-derived products. The statutory price ceilings in negotiation are above or in line with the effects of generic and biosimilar competition for such products over time, which ensures that negotiated prices do not fall below the margins required to maintain their production.

Section 60.5.1. Application of the MFP to New NDAs/BLAs or NDCs

We strongly support CMS' determination that formulations of a selected drug marketed under a new NDA or BLA will be subject to the MFP in Sec. 60.5.1. Doing so ensures that savings from negotiation are not undermined by the availability of direct substitutes to a selected drug that are not subject to the MFP.

Because new NDAs and BLAs are often associated with reformulation strategies, we anticipate that some manufacturers will argue that this decision discourages the development of new formulations of products for the treatment of new indications, which could not be accomplished through older formulations. This argument ignores two important realities. One is that the level of scientific innovation and risk of developing older products for new indications is substantially lower than developing a new active ingredient or moiety. The other is that, in making an exemption for new formulations intended for new indications, CMS would be disadvantaging the development of older formulations for new

¹ Congressional Budget Office. Estimated Budgetary Effects of Public Law 117-169. Available from: https://www.cbo.gov/system/files/2022-09/PL117-169_9-7-22.pdf. Accessed 4/10/2023.

² Hartmann J, Klein HG. Supply and demand for plasma-derived medicinal products - A critical reassessment amid the COVID-19 pandemic. *Transfusion*. 2020 Nov;60(11):2748-2752. doi: 10.1111/trf.16078. Epub 2020 Sep 9. PMID: 32856742; PMCID: PMC7460929.

indications, which can be equally valuable for patients. In fact, the number of NDAs and BLAs for a particular active ingredient or moiety makes a poor measure of most aspects of a branded drug's life cycle. Manufacturers can and do market multiple brands of an active ingredient or moiety under the same NDA or BLA, as well as multiple formulations and indications. However, they also do the same under multiple NDAs and BLAs.

Recommendation: Maintain the decision under Section 60.5.1 to apply a selected drugs' MFP to any of its new NDAs and BLAs

We strongly urge CMS to maintain the decisions it has made with respect to its treatment of multiple NDAs and BLAs. We believe that the proposed policy is in line with Congress' intent to negotiate what Medicare pays for older drugs, including their various reformulations and new indications added later in their life cycle on the market.

Managing information submitted by manufacturers

Section 40. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026

CMS requests comments on its proposed policy for confidentiality of proprietary manufacturer data in Section 40.2.1, to treat as proprietary any information submitted by manufacturers that cannot be found publicly.

Recommendation: Revisit the classification and handling of proprietary data in coming years

Although we acknowledge the need for confidential handling of sensitive data from manufacturers, we are concerned that this creates a lack of transparency, and limits the ability for public and Congressional oversight. At a minimum, we encourage CMS to revisit this approach in coming years, and to re-evaluate whether this approach should be applied to a more narrow set of data elements.

Recommendation: Require word-limited executive summaries of submissions

To facilitate its review of manufacturer data, we suggest that CMS require an executive summary of data and materials to be included in manufacturer submissions, subject to a pre-specified word limit. CMS should set expectations that this summary may be audited against the underlying data after negotiation is completed. CMS should also specify that the executive summary must accurately represent the underlying data in the manufacturer's submission, and that misrepresentations may constitute a violation of Sec. 1193(a)(4)(B) of the Act, and thus subject to Civil Monetary Penalties under Sec. 1197(b).

Recommendation: Verify proprietary data using public sources

We also urge CMS to consider public sources to verify the manufacturers' submissions. Publicly traded companies, for example, disclose R&D expenditures in SEC filings and earnings releases. They also include details of other economic transactions that factor in R&D expenses, such as mergers and acquisitions and licensing fees. Although this information may not break down to the level of an individual drug, it may offer a sense of the upper bound of R&D investment for a particular drug, against which manufacturer numbers may be gauged.

Recommendation: De-emphasize distribution costs

We suggest that CMS de-emphasize distribution costs in the information it receives from manufacturers. Costs of distribution to the manufacturer are both small and difficult to quantify. Companies sell their products (frequently at a discount) to wholesalers and distributors, who then mark up the drug and sell it to pharmacies or other purchasers. As a result, distribution costs are generally borne by purchasers through spread pricing and are not paid for directly by the manufacturers. We also note that, although manufacturing costs are borne directly by the manufacturers and are more straightforward to quantify, they are generally a small percentage of sales for the top-selling mature products that are likely to be candidates for negotiation.

Managing and evaluating data on therapeutic alternatives

Summarizing data

CMS can expect to receive a substantial amount of data, both from manufacturers entering into agreements under Sec. 1193 of the Act, and other stakeholders providing input on therapeutic alternatives per Section 50.2 of the guidance. It is unlikely that the agency will be able to fully review and interpret each piece of information it receives through these channels before negotiations begin.

Recommendation: Require word-limited executive summaries of submissions

As with manufacturer submissions, CMS should require a word-limited executive summary for any submissions by the public on therapeutic alternatives, to assist in rapidly processing and prioritizing the underlying information.

A heuristic for evaluating submitted data

Recommendation: Systematically prioritize and weigh evidence according to its quality and likelihood of bias

In order to process the data CMS receives from manufacturers and the general public in the requisite amount of time, we strongly recommend that CMS prioritizes its review of submissions with the lowest likelihood of bias and the highest quality of evidence. CMS should consider established standards for evidence evaluation in developing a means of prioritizing information received. A significant body of work exists for evaluating evidence quality, and covers a variety of study types, including clinical trials, observational studies, and systematic reviews and meta-analyses. As a starting point for developing a systematic means of weighing the importance of specific types of data, CMS should consider the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework, which promulgates best practices for grading evidence, and the Institute for Clinical and Economic Research Evidence Rating Matrix.^{3,4}

To implement a systematic process in time to develop an offer, we also recommend that CMS add several requirements for data submitted by manufacturers and the public, or state that they will

³ BMJ Best Practice. What is GRADE? Available from: <https://bestpractice.bmj.com/info/us/toolkit/learn-ebm/what-is-grade/#:~:text=GRADE%20has%20four%20levels%20of,data%20starts%20at%20low%20quality>. Accessed 4/13/2023.

⁴ Institute for Clinical and Economic Review. ICER Evidence Rating Matrix: A User's Guide. Available from: <https://icer.org/wp-content/uploads/2020/10/Rating-Matrix-User-Guide-UPDATED-06.30.17.pdf>. Accessed 4/14/2023.

prioritize submissions that meet certain reporting requirements documenting the likelihood of bias and quality of evidence that they contain.

Likelihood of bias

Recommendation: Require disclosure of financial conflicts of interest for stakeholders submitting evidence

In order to evaluate bias, CMS should require conflict of interest information from individuals or groups submitting information per Section 50.2 of the guidance or announce that it will prioritize submissions with such disclosures. Research suggests that financial and other conflicts of interest can have a considerable effect on how individuals perceive, interpret, and present information.⁵ This is well known in the scientific community, and is why all leading peer-reviewed journals require authors to disclose conflicts of interest. However, the problem is not limited to scientific studies, and has been found to extend to provider prescribing behavior as well as patient advocacy positions.^{6,7}

Requiring disclosure of conflicts of interest will allow CMS to gauge the probability and direction of bias in the development and selection of the submitted evidence.

Evidence quality

Recommendation: Align submission standards with established data reporting guidelines

We anticipate that data on therapeutic alternatives submitted to CMS will come from multiple different types of studies, each of which with their considerations and potential sources of bias. CMS can simplify the process of evaluating this evidence by drawing on several frameworks that provide valuable insight about signifiers of scientific rigor and sources of bias for different types of research.

The Consolidated Standards of Reporting Trials (CONSORT) and Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT), for example, provide guidelines for the reporting of clinical studies, including randomized controlled trials.⁸ Similarly, Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines are available for observational studies.⁹

CMS will likely also receive submissions that include literature reviews and meta-analyses. When done systematically and according to best practices, such reviews can provide valuable insights, such as

⁵ Kjaergard LL, Als-Nielsen B. Association between competing interests and authors' conclusions: Epidemiological study of randomised clinical trials published in the BMJ. *BMJ*. 2002;325:249.

⁶ Mitchell AP, Trivedi NU, Gennarelli RL, Chimonas S, Tabatabai SM, Goldberg J, Diaz LA Jr, Korenstein D. Are Financial Payments From the Pharmaceutical Industry Associated With Physician Prescribing? : A Systematic Review. *Ann Intern Med*. 2021 Mar;174(3):353-361. doi: 10.7326/M20-5665. Epub 2020 Nov 24. PMID: 33226858; PMCID: PMC8315858.

⁷ Kaiser Health News. Patient Advocacy Groups Take In Millions From Drugmakers. Is There A Payback? Available from: <https://kffhealthnews.org/news/patient-advocacy-groups-take-in-millions-from-drugmakers-is-there-a-payback/>. Accessed 4/13/2023.

⁸ Hopewell, S., Boutron, I., Chan, AW. et al. An update to SPIRIT and CONSORT reporting guidelines to enhance transparency in randomized trials. *Nat Med* 28, 1740–1743 (2022). <https://doi.org/10.1038/s41591-022-01989-8>

⁹ von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007 Oct 20;370(9596):1453-7. doi: 10.1016/S0140-6736(07)61602-X. PMID: 18064739.

whether results are replicable across different clinical trials.¹⁰ However, like clinical studies, reviews and meta-analyses can also vary in quality and suffer from biases, which are particularly difficult to assess because of the large number of studies that may be included or excluded. To address this concern, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework a systematic means of documenting and interpreting systematic literature reviews and meta-analyses.¹¹

Each of these frameworks, and others like them, are accompanied by check lists that can be filled out by researchers to succinctly describe how their studies are designed and to document potential sources of bias. To facilitate the rapid evaluation of evidence quality and bias, we strongly recommend that CMS either require submissions of studies on therapeutic alternatives to include completed checklists, or indicate that it will prioritize its review of submissions containing completed checklists.

Recommendation: CMS should prioritize evidence of direct health benefits to patients

In addition to considering evidence quality and bias, CMS should prioritize evidence that describes the extent to which a given treatment improves health outcomes. Recent years have seen a significant push to consider additional measures of treatment benefit in health technology assessment (HTA). Proponents of this work contend that existing approaches do not capture all elements of a drug's value, such as benefits to caregivers, variations in risk acceptance among different patients (e.g., "the value of hope"), scientific spillover effects, and other possible domains of value, many of which are now described in what has become known as the "ISPOR value flower".¹²

We anticipate that CMS will receive a significant amount of input in this vein, and recommend that it be disregarded or de-prioritized relative to direct measures of health benefits. This is for two reasons. The first is that most, if not all, of the proposed additional measures of value can be achieved through means other than pharmaceutical treatment. Including them therefore opens the door to considering non-pharmacological and even non-medical interventions. For example, productivity could also be achieved through investment in education or transportation. However, these types of intervention do not fall within CMS' decision-making authority or remit. Considering such a measure would, in our view, be inappropriate in this context. Secondly, assigning value to prescription drugs in addition to their health benefits creates scenarios in which drugs that have no meaningful health benefits can nevertheless demand high prices. Healthcare systems, however, are meant to pay for treatments that work.¹³ CMS, which pays for treatments that are "reasonable and necessary" should be no exception.

¹⁰ Siddaway AP, Wood AM, Hedges LV. How to Do a Systematic Review: A Best Practice Guide for Conducting and Reporting Narrative Reviews, Meta-Analyses, and Meta-Syntheses. *Annu Rev Psychol.* 2019 Jan 4;70:747-770. doi: 10.1146/annurev-psych-010418-102803. Epub 2018 Aug 8. PMID: 30089228.

¹¹ <http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1>

¹² Lakdawalla et al. Defining Elements of Value in Health Care—A Health Economics Approach: An ISPOR Special Task Force Report. Available from: [https://www.valueinhealthjournal.com/article/S1098-3015\(17\)33892-5/fulltext?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1098301517338925%3Fshowall%3Dtrue](https://www.valueinhealthjournal.com/article/S1098-3015(17)33892-5/fulltext?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1098301517338925%3Fshowall%3Dtrue). Accessed 4/13/2023.

¹³ Morton A. Treacle and Smallpox: Two Tests for Multicriteria Decision Analysis Models in Health Technology Assessment. *Value Health.* 2017 Mar;20(3):512-515. doi: 10.1016/j.jval.2016.10.005. Epub 2016 Dec 20. PMID: 28292498.

Recommendation: Consider cost-benefit and cost-effectiveness analyses, particularly for drugs with no therapeutic alternatives

As the guidance notes, CMS will not use the Quality Adjusted Life Year (QALY), and CMS seeks input on what other measures that might treat the life of an older person, someone who is disabled, and someone who is terminally ill as of lower value than that of a healthy peer.

We view these concerns as misplaced, particularly in the context of negotiation, which will have the effect of increasing such patients' access to drugs. Selected drugs cannot be excluded from formularies, and reductions in what Medicare and its beneficiaries pay for them further increase access and affordability. There are powerful safeguards in place to ensure that negotiations will not result in loss of coverage for selected drugs. These include ceiling prices calibrated on generic and biosimilar competition, as well as concrete measures of manufacturer costs described in Sec 1194(e), which will prevent CMS from making offers below the point of a drug's economic viability. Perhaps more importantly, manufacturers can credibly threaten to withdraw their drugs from all Federal programs if they cannot profitably continue to offer a selected drug under Medicare coverage. In fact, the CBO considers this threat to be such a challenge to Medicare's negotiating leverage that it has historically estimated that negotiation proposals without consequences for manufacturers would result in no savings.¹⁴

Given this context, we believe that there is virtually no risk that negotiation will diminish access to selected drugs or their alternatives, and thus no risk to patients with health disadvantages in considering systematic measures of health benefits. There are substantial advantages to considering systematic measures such as Equal Value of Life Years Gained (evLYG) or Disability-Adjusted Life Years (DALYs), which is that they efficiently encapsulate multiple types of health benefits into one summary measure. As such, we strongly recommend that CMS consider cost-effectiveness and cost-benefit analyses that use summary measures such as the evLYG or DALY.

Developing price offers

Recommendation: Develop starting and counteroffers for drugs without therapeutic alternatives based on cost-effectiveness and what would occur under competition

In 60.3.2, CMS outlines plans to use as a starting point the net prices for drugs with one therapeutic alternative, and prices achieved by the Big Four Price as the starting point for drugs without therapeutic alternatives. We support the use of net prices in the case of a therapeutic alternative because plans have the ability to use competition between drugs to demand a lower price. However, we recommend against using Big Four prices as an offer benchmark for drugs without therapeutic alternatives. This is because the negotiating power of the Big Four relies not on their ability to make drugs compete, but on their ability to exclude them from formularies. Because Medicare covers significantly more beneficiaries than the Big Four, we expect that manufacturers of drugs with no therapeutic alternatives will become less willing to offer significant price concessions to the Big Four, as it would erode their starting point in negotiation with CMS. We suggest that instead, CMS consider studies of net price reductions that occur with the introduction of competition, such as from generics, biosimilars, or new therapeutic

¹⁴ Congressional Budget Office. RE: Negotiation Over Drug Prices in Medicare. Available from: <https://www.cbo.gov/system/files/2019-05/55270-DrugPricesMedicare.pdf>. Accessed 4/12/2023.

alternatives. Estimates from these studies can be used to impute what the price of a selected drug would be if it had competition. Alternatively, or in addition, CMS could consider estimates of the drug's cost-effectiveness or cost-benefit, using measures such as the evLGY, setting a threshold for an acceptable cost-benefit ratio and imputing the price at which the drug would meet the threshold.

Recommendation: Do not treat small molecules and biologics differently in negotiation

Pharmaceutical industry stakeholders have argued that the structure of the Act disadvantages small molecules relative to biologics because they may be selected sooner. We anticipate that they will propose policies to favor small molecules in negotiation, such as limiting offers to the statutory price ceilings for small molecules or delaying their renegotiation as they qualify for extended and long monopolies.

We strongly urge CMS to disregard these proposals. There is no support for such distinctions in the Act, which is consistent with a long history of Congressional decisions to treat these two types of drugs differently, including patent and exclusivity protections set forth in Hatch-Waxman and the Biologics Price Competition and Innovation Act (BPCIA).^{15,16} Abuses of these protections have contributed significantly to lengthy delays in generic and biosimilar entry, leading to high and rising prices for the older drugs that are likely to be selected for negotiation. The question of whether to treat small molecules and biologics at parity across the different laws that do not is one that can only be answered by Congress.

Monitoring bona fide marketing

We strongly support CMS' policy of monitoring uptake of generic and biosimilar to verify that marketing of these products is bona fide and will result in savings to Medicare and its beneficiaries, and offer several recommendations to strengthen this approach.

Recommendation: Require manufacturers to attest or provide proof of full market entry

CMS should require manufacturers of the selected drug and its generic or biosimilar demonstrate that they have not entered into an agreement to allow for limited marketing of the generic or biosimilar.

This could take the form of requiring them to attest that they have not entered into any agreements that would limit the market share of the generic or biosimilar products, either implicitly or explicitly. In addition, CMS could require manufacturers to submit all agreements provided to the Federal Trade Commission (FTC), as they would under a biosimilar delay request, which would allow CMS to evaluate the terms directly.

In addition, CMS should include terms requiring the submission of such manufacturer agreements under Section 1193(a)(5) of the Act as part of Medicare requirements to administer the program and monitor it for compliance.

¹⁵ Pub.L. No. 98-417.

¹⁶ Pub. L. No. 111-148.

Recommendation: CMS should monitor generic/biosimilar uptake across all US payers

To ensure that generic and biosimilar uptake of a selected drug is not being limited, CMS should also monitor uptake across the US market more broadly and compare these rates with those being achieved by Medicare.

In general, this exercise will be more straightforward for generics, which have a long enough history on the market to have been studied extensively. CMS could consider a drug to have been effectively marketed, for example, if its market share is demonstrably within a standard deviation of the mean for a given period of time since market entry, and/or if it is at or above the mean of uptake at the point of CMS having to make a decision about whether the branded drug remains selected.

Guiding Part D formulary management of selected drugs

CMS should consider requiring that Part D plans place selected drugs on lower or equivalent tiers than their competitors and limit utilization management strategies such as prior authorizations or step edits for selected drugs, unless plans achieve lower net prices on competitor products, or competitor products reduce their list prices to below a selected drug's MFP. This has the benefit of encouraging competition among therapeutic alternatives to selected drugs, which Part D plans are well positioned to manage. It also aligns with existing formulary rules promulgated by CMS, such as required coverage of protected classes of drugs, and rules for generic and specialty tiers. These requirements set an important precedent for the policy we suggest here, which is that they have not been deemed violations of the non-interference clause.

April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health & Human Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Re: Medicare Drug Price Negotiation Program Guidance: Initial Memorandum, Implementation of Section 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Seshamani,

As the world's leading nonprofit organization dedicated to autoimmune disease advocacy, awareness, education, and research, the Autoimmune Association appreciates the opportunity to respond to the Centers for Medicare and Medicaid Services' initial draft guidance detailing the requirements and parameters for the new Medicare Drug Negotiation Program.

People living with autoimmune diseases face unique challenges in their day-to-day lives and depend on novel and innovative treatments to successfully manage their conditions. The Inflation Reduction Act's drug pricing provisions will have wide-ranging implications for not only Medicare beneficiaries, but all autoimmune patients who stand to benefit from innovative therapies that are currently on the market, as well as those in the development pipeline.

As the agency moves to implement this and future program guidance, we urge policymakers to remain vigilant of potential unintended consequences that could jeopardize future patient access to these therapies.

We would like to call your attention to the following components of the draft guidance which are of particular concern to us.

The Medicare Drug Price Negotiation Program should consider patient access beyond coverage requirements.

Coverage is only one component of access. As an organization dedicated to advancing policies that improve the health and well-being of people living with autoimmune disease, the Autoimmune Association is particularly attuned to the impacts of payer-imposed access barriers on patients. Through our Let My Doctors Decide initiative, we recently rolled out a national scorecard assessing the extent to which insurers – including Medicare Advantage and Part D prescription drug plans – and their pharmacy benefit managers restrict access to medications to manage some of the most common autoimmune diseases affecting an estimated 15.9 million Americans.¹ The scorecard looked at three types of utilization management tactics employed by payers: step therapy, prior authorization, and restrictive formulary placement.

The results were not promising. Few – if any – plan types received a “A” grade under our criteria. Across all conditions, nearly half of all Medicare Advantage and Part D plans achieved a failing score and nearly 9 in 10 plans scored a C or worse.

With close to half of all Medicare beneficiaries now enrolled in a Medicare Advantage plan, and approximately 47% enrolled in a standalone Part D plan, changes to how the Medicare program pays for prescription drugs will have major implications for this subset of the Medicare population.

¹ Health Insurance Access Barriers: A National Scorecard. January 2023. Let My Doctors Decide. Accessed: <https://autoimmune.org/healthplanscorecard/>

As it implements this and future guidance, we encourage CMS to consider the impact of payer benefit design on patient access in addition to requiring coverage for treatments within the Drug Price Negotiation Program.

CMS definition of “unmet medical need” is too narrow

In section 1194(e)(2) of the IRA legislation, CMS is required to consider the extent to which a drug fulfills an “unmet medical need” as part of the negotiation process. However, in the guidance, CMS states its intention to define unmet medical need as treating “a disease or condition in cases where **very limited or no other treatment options exist.**”

We believe CMS’ interpretation of unmet medical need is too narrow and may not be entirely consistent with how it is referenced in 1194(e)(2): “The extent to which the selected drug and the therapeutic alternative to the drug address unmet medical needs for a condition for which treatment or diagnosis is not addressed **adequately** by available therapy.”

“Adequacy” in this context of unmet medical need is a much broader concept than the mere availability of a treatment option. **We recommend CMS adopt a broader definition of unmet medical need that reflects the diversity of patient preferences and needs.** This was the approach taken in the authorizing statutes of the Patient-Centered Outcomes Research Institute which established a more comprehensive approach to evaluating unmet medical needs that included the consideration of “needs, outcomes and preferences” of patients.²

For example, a person living with an autoimmune condition might prefer a treatment with fewer side effects or that is easier or more conveniently to administer over one with a slightly higher clinical benefit. To this patient, the quality-of-life improvement from reduced side effects and/or not having to frequently travel to receive a more invasive treatment may weigh heavier in their personal calculation of value than the availability of another treatment. CMS’ current definition of unmet medical need in the guidance is not reflective of this heterogeneity of preferences which will have major ramifications for how it will evaluate treatments in the negotiation process.

The implementation of program guidance must be more inclusive of patients, families and caregivers.

CMS has stated intention to include the “patient experience” in the development of program guidance and has signaled a willingness to solicit and consider feedback from a wide range of stakeholders in implementing the Medicare Drug Negotiation Program.

But the short, 30-day timeframes allotted for stakeholders to respond to this and future guidance documents renders this process difficult and severely limits the opportunity for the patient community to meaningfully engage.

We urge the agency to allow for more time for community feedback throughout the implementation of this program moving forward. We believe expanded opportunities for public comment will enhance future program development and could potentially help the agency avoid unintended consequences that could undermine patient access to needed therapies.

Thank you for your consideration and for the opportunity to weigh in on this draft guidance document. Please contact Christian Miller at christian@autoimmune.org should you have any further questions.

Sincerely,

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² 42 USC Sec 1320e(d)(1)(A)



Via Electronic Submission

April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator, Director of the Center for Medicare
Centers for Medicare & Medicaid Services
200 Independence Avenue SW
Washington, DC 20201

Subject: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Dr. Seshamani,

Bayer US (“Bayer”) appreciates the opportunity to offer its input to the Centers for Medicare and Medicaid Services (CMS) initial memorandum issued March 15, 2023, regarding the drug price setting program implementing provisions of the Inflation Reduction Act.

Bayer is a global enterprise with core competencies in the Life Science fields of health care and agriculture with nearly 25,000 employees in 300 sites across the United States. Our products and services are designed to benefit people and improve their quality of life. At the same time, we aim to create value through innovation and are committed to the principles of sustainable development and to our social and ethical responsibilities as a corporate citizen.

Certainly, there are many unanswered questions about the implementation of the Inflation Reduction Act (IRA). The drug price program has significant implications for the future of innovation in the United States, heightening the importance of the implementation of these provisions. Thus, the application of administrative discretion as allowed under the statute is essential in ensuring that the program is implemented in a manner that avoids unintended consequences and preserves innovation for critical medical conditions, including new treatments for patients with cancer or rare medical conditions to those chronic diseases for which new medical treatments are needed.

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April 14, 2023

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The enactment of Medicare Part D in 2003 ushered in an era of meaningful gains in life expectancy and quality of life for older Americans. Yet today's Medicare patients continue to face unmet medical needs. With more than 400 medicines under development for leading chronic diseases impacting older Americans, it is vital that implementation of the IRA's negotiation provisions allows innovation to continue.¹

We address several topics of particular importance to Bayer in this letter. The comments are offered in the hope of ensuring better access to important new treatments to patients.

Comment Overview: Following is a summary of our feedback provided in this document.

Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026

- I. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026: Primary v Secondary Manufacturers (40.):** We support an approach that confirms the proposed obligation that a Primary Manufacturer be responsible for a Secondary Manufacturer *only exists* when there is contractual understanding and commitment between the two entities. We request confirmation of this interpretation.
- II. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026: Manufacturer Agreements (40.1):** We are concerned about a 5-day review time for a manufacturer agreement and point to other approaches used for initiation of programs, such as the agreement for the Medicare Part D Coverage Gap. Furthermore, we believe manufacturers should have ample opportunity to review and comment on a draft version of the Agreement.
- III. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026: Confidentiality of Proprietary Information (40.2.1; 50.1; Appendix C):** We support CMS using Exemption 4 of the Freedom of Information Act (FOIA) related to confidential information from manufacturers. Furthermore, we believe manufacturers should be allowed to designate its information as confidential to the extent that it cannot legally be found publicly. In addition, the guidance should not override the full range of other potentially applicable privacy and confidentiality laws, including but not limited to the Trade Secrets Act and the Tax Reform Act.
- IV. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026: Data Use Provisions and Limitations (40.2.2):** We have several reservations about the provisions of this section as they pertain to data use and limitations that should be addressed and revised by CMS. This includes concerns about the 5-day review of an Agreement governing those limitations without an opportunity for input. Furthermore, we find the proposed approach largely one-sided in which CMS would be allowed to disclose certain data shared as part of the process, but the manufacturer would not be allowed to respond based on information considered during the discussions of the set price. Also, once

¹ PhRMA. Fact Sheet: *Addressing the Unmet Medical Needs of Older Americans*. Accessed April 3, 2023 at: <https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Refresh/Fact-Sheets/A-C/Addressing-the-Unmet-Medical-Needs-of-Older-Americans-2.pdf>

the selected drug status no longer applies, we believe a 30-day requirement to destroy all data pertaining to a negotiation is unworkable.

- V. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026: Providing Access to the MFP (40.4):** CMS lays out requirements for manufacturers to ensure the MFP for a selected drug is available to pharmacies, mail order services, and other dispensers with respect to MFP-eligible individuals under Part D in a 14-day period. This should be clarified so the 14 days do not begin until the claim is verified and adjudicated as a “clean claim.” We also recommend that CMS use an approach similar to the Medicare Part D Coverage Gap discount program, inclusive of using a third-party administrator, to implement these provisions.

Negotiation Factors

- VI. Manufacturer-Specific Data: Data Elements and Consideration of Manufacturer-Specific Data (50.1; 60.3.4):** As a general matter, we believe that the submission of data by manufacturers to CMS should not be limited to a one-time submission. Manufacturers should be able to amend their submissions to CMS as additional relevant information becomes available. In addition, we offer several recommendations pertaining to data for research and development (R&D) costs, information on pending and approved patent applications, regulatory exclusivities, a net price calculation and tax credits.
- VII. Manufacturer-Specific Data: Evidence About Therapeutic Alternatives for the Selected Drug (50.2):** We believe identification of therapeutic alternatives must be done by CMS in a public manner allowing for comments from the manufacturer and other key stakeholders. We also offer recommendations for the determination of a therapeutic advance or a medication addressing an unmet medical need based on examples from the Food and Drug Administration, the Medicare New Technology Add-on Payment (NTAP) and guidelines from the National Comprehensive Cancer Network (NCCN).

Negotiations

- VIII. MFP Ceiling Price (60.2):** We believe there are several instances in which CMS should consider a maximum fair price (MFP) that is set no lower than the ceiling price. The first approach is for small molecules at least up until their 13th year post-approval to ensure adequate time for these treatments to generate sufficient revenues to incentivize ongoing research. In addition, we recommend a ceiling price minimum for medications deemed as offering a significant therapeutic advance or addressing an unmet medical need inclusive of noted examples from the FDA, NTAP program or NCCN.
- IX. Negotiation Process (60.4):** We recommend CMS define its approach to meetings for which a 3-meeting limit is proposed. To that end, an approach comparable to that used by the FDA should be considered in which there are tiers of meetings described. For purposes of application by CMS, only the highest-level meetings would be recognized as counting toward the limit during which time specific information to support an offer or counteroffer discussion would apply.

Compliance and Penalties

- X. Manufacturer Compliance and Oversight (90):** We appreciate that CMS is looking to establish a robust and fair process for reporting of violations. For the process to be fair and equitable, we believe that such a reporting process should be developed hand in hand with a robust dispute resolution process. CMS should undertake notice and comment rulemaking to establish such reporting of violations and dispute resolution, similar to the process that was used in establishing the recent 340B Program's dispute resolution process.
- XI. Civil Monetary Penalties (100):** We believe the excessive penalties provided in Section 1197 that authorizes extraordinarily high CMP penalties equal to \$100 million for each item of false information and \$1 million per day for failing to provide the information required under section 1193(a)(4) warrant notice-and-comment rulemaking prior to Agency implementation. In addition, as part of the dispute resolution process, the manufacturer should be able to raise as a defense, that the violation at issue was committed by a third party and not by the manufacturer. We urge CMS not to impose CMPs on drug manufactures for unrelated third-party non-compliance. Given the excessive fines and penalties that may be imposed, we strongly urge CMS to adopt the 'actual knowingly' standard, which would eliminate doubt as to the intent and awareness of the party performing the act.

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Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026

I. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026: Primary v Secondary Manufacturers (40.)

The CMS definition of a "Primary Manufacturer" refers to a description where "...more than one entity meets the statutory definition of Manufacturer for a selected drug..." CMS goes on to state that it, "...intends to refer to any other entity that meets the statutory definition of manufacturer for a drug product included in the selected drug and that either (1) is listed as a manufacturer in an NDA or BLA for the selected drug or (2) markets the selected drug pursuant to an agreement with the Primary Manufacturer." Entities falling into category 2 are defined as "Secondary Manufacturers" and would be impacted by negotiation if the Primary Manufacturer is selected.

We understand that the application of the term "Secondary Manufacturer" could be applied to an authorized generic manufacturer, repackager or relabeller of a selected drug. In this instance, it is the Primary Manufacturer that is responsible for engaging in negotiation and meeting CMS requirements, including requirements for any Secondary Manufacturers. We note the definition cited above mentions an agreement, and concur that a Primary Manufacturer could *only* be responsible for other entities if an agreement exists between the Primary Manufacturer and these other entities. Thus, we are seeking to confirm our understanding of the situation as

responsibility for the requirements for the Primary Manufacturer outlined in this section would be impossible to enforce without such an agreement.

We agree and urge CMS to support an approach that confirms the obligation being imposed upon a Primary Manufacturer *only exists* when such a contractual understanding and commitment exists between a Primary Manufacturer and a Secondary Manufacturer. Any other obligation beyond those terms would be impossible for a Primary Manufacturer to compel or enforce.

II. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026: Manufacturer Agreements (40.1)

CMS notes in section 40.1 that it intends to enter into an Agreement with manufacturers of selected drugs for the initial price applicability year (2026), with a deadline of October 1, 2023. It is noted that manufacturers will have 5 days following publication of the selected drug list to sign an Agreement with CMS. This will include all names, titles and contact information for representatives authorized to execute the Agreement who are “...legally authorized to bind the Primary Manufacturer to the terms and conditions of the Agreement.” At least one of the representatives must sign the agreement using the CMS HPMS. In addition, CMS indicates it “...does not intend to enter into an Agreement with any Secondary Manufacturer of a selected drug,” and further that “...CMS intends to include in the Agreement with the Primary Manufacturer several requirements pertaining to Secondary Manufacturers of the selected drug.”

CMS states it “...will make reasonable efforts to make the final text of the Agreement available to the public before the selected drug list for initial price applicability year 2026 is published.” However, it is not clear when or if this effort will be achieved prior to the publication date.

Failure to adhere to the provisions of the IRA come with significant statutory penalties, inclusive of severe excise taxes. Given the magnitude of the penalties, it is critical to understand whether and how they would apply regarding the signing of this manufacturer Agreement. For example, what if the Primary Manufacturer is unable to meet the 5-day deadline with respect to itself or its Secondary Manufacturers? It is important to note that October 1, 2023, is a Sunday. Thus, this potentially shortens the review time to just 3 or 4 days, for a major corporate decision, potentially involving outside entities like Secondary Manufacturers, on an Agreement for which they had no opportunity to review. Further clarity on the timing and opportunity for review of a draft agreement, and consideration of a grace period at least in the program’s first year, would be helpful from the agency.

Current approaches to price-related contracting by the government are instructive.

National Drug Rebate Agreement: As an example, the Federal Medicaid National Drug Rebate Agreement (NDRA) has no specific time to enter into an Agreement.² Manufacturer medications are not covered until an Agreement is signed. Once signed, the labeler codes become mandatorily covered on the first day of the calendar quarter that begins more than 60 days after the date of the completed and signed NDRA. States can optionally cover drugs based on the date the NDRA is signed. As noted, the last date on which a new manufacturer's rebate Agreement can be accepted to establish the mandatory state coverage date each quarter (in a non-leap year) is as follows:

For a Mandatory Effective Date of:	The Rebate Agreement Must Be Received and Accepted by CMS by:
1st Quarter (i.e., January 1st)	November 1
2nd Quarter (i.e., April 1st)	January 30
3rd Quarter (i.e., July 1st)	May 1
4th Quarter (i.e., October 1st)	August 1

The penalty for not signing the NDRA is failure to require coverage of medications for a manufacturer. However, with the Medicare program, the penalty could ultimately be an excise tax valued at approximately 1,900 percent.

Medicare Part D Coverage Gap Discount: Section 423.2315(c) of the Medicare Coverage Gap Discount Program regulations specified timing requirements for the program. In addition, CMS and manufacturers worked together, well in advance, on the Agreement for the program. By the time the program launched in 2011, manufacturers were familiar with the terms of the Agreement. The language in the rule is as follows:

§ 423.2315 Medicare Coverage Gap Discount Program Agreement.³

(c) Timing and length of agreement.

- (1) For 2011, a manufacturer must enter into a Discount Program Agreement not later than **30 days** after the date of establishment of the model Discount Program Agreement. [emphasis added]
- (2) For 2012 and subsequent years, for a Discount Program Agreement to be effective for a year, a manufacturer must enter into a Discount Program Agreement not later than January 30th of the preceding year.
- (3) Unless terminated in accordance with § 423.2345, the initial period of a Discount Program Agreement is 24 months and the agreement is automatically renewed for a 1-year period on January first each year for a period of 1 year thereafter.

² Centers for Medicare and Medicaid Services. *Medicaid National Drug Rebate Agreement (NDRA)*. Accessed March 27, 2023 at: <https://www.medicare.gov/medicaid/prescription-drugs/medicaid-drug-rebate-program/medicaid-national-drug-rebate-agreement-ndra/index.html>

³ 42 C.F.R. 423.2315 Accessed March 27, 2023 at: <https://www.ecfr.gov/current/title-42/chapter-IV/subchapter-B/part-423/subpart-W>

Veterans Affairs and the Federal Supply Schedule: The Department of Veterans Affairs (VA) manages the pharmaceutical portion of the Federal Supply Schedule (FSS) for the General Services Administration (GSA). Contracting is based on the submission of offers by manufacturers. Under this program, there is no set timetable for the submission of offers as noted by the Vendor Response Document.^{4,5}

Summation: We recognize that the programs discussed above are different and unique in the context of the IRA drug price negotiation process. Irrespective, the processes in use for other programs, in the very least suggests the need for a longer review time than 5 days. Thus, availability of at least a draft version of the Agreement is important in the proper implementation of this program moving forward.

III. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026: Confidentiality of Proprietary Information (40.2.1; 50.1; Appendix C)

Overall, section 1193(c) of the Inflation Reduction Act (IRA) specifies Congress' intent to protect from public release any confidential information provided by manufacturers to HHS in the context of maximum fair price negotiations. This was the subject of multiple discussions with key officials in IRA negotiations and is a central feature of the statute, not an afterthought.

The statute provides the following:

(c) CONFIDENTIALITY OF INFORMATION.—Information submitted to the Secretary under this part by a manufacturer of a selected drug that is proprietary information of such manufacturer (*as determined by the Secretary*) shall be used only by the Secretary or disclosed to and used by the Comptroller General of the United States for purposes of carrying out this part.

While the statute grants the Secretary authority to determine whether specific information is proprietary, it does not waive other applicable laws that would protect manufacturer information from disclosure. Thus, the Secretary must implement section 1193(c) considering existing law, practices, and procedures. Of note, both CMS and the Food and Drug Administration (FDA) routinely make determinations about proprietary information release already, under processes established through notice and comment rulemaking. These approaches supplement the overarching HHS procedures found at 45 C.F.R. Part 5.^{6,7,8}

⁴ US Department of Veterans Affairs. Office of Procurement, Acquisition and Logistics (OPAL). *Schedule 65 I B Drugs, Pharmaceuticals, & Hematology Related Products*. Accessed March 27, 2023 at: <https://www.va.gov/opal/nac/fss/pharmaceuticals.asp>

⁵ US Department of Veterans Affairs. *02 – VENDOR RESPONSE DOCUMENT*. MS-Q50A-03-R8. Accessed March 27, 2023 at: <https://www.va.gov/opal/docs/nac/fss/vaSolicitationM5Q50A03R8.zip>

⁶ 42 C.F.R. Part 401 – General Administrative Requirements. Subpart B – Confidentiality and Disclosure. Accessed March 31, 2023 at: <https://www.ecfr.gov/current/title-42/chapter-IV/subchapter-A/part-401>

⁷ 21 C.F.R. Part 20 – Public Information. Accessed March 31, 2023 at: <https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-20>

⁸ 45 C.F.R. Part 5 – Freedom of Information Regulations. Accessed April 6, 2023 at: <https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-5>

The negotiation process requires manufacturers of selected drugs to submit extensive information, including information not currently compiled today and certainly not public. We are pleased that CMS notes an intention to treat much of these data as proprietary, with a reference to Exemption 4 of the Freedom of Information Act (FOIA). However, we note a desire of CMS to “strike an appropriate balance between (1) protecting the highly sensitive information of manufacturers and ensuring that manufacturers submit the information CMS needs for the Negotiation Program, and (2) avoiding treating information that does not qualify for such protection as proprietary.”⁹ This test raises some questions given long-standing protections for confidential information in the hands of government officials and government employees. We question whether it is needed or appropriate.

We support a test of information being proprietary if the information cannot be found publicly, and we are pleased to see a test like this adopted in the guidance. We would like to clarify that manufacturers would have the opportunity to designate its information as proprietary or confidential, and then the responsibility for proving that information is public would sit with CMS. We also would like to clarify that nothing in the guidance overrides the full range of other potentially applicable privacy and confidentiality laws.

In addition to FOIA, the Trade Secrets Act is a criminal statute that prohibits government disclosure of information that “concerns or relates to the trade secrets, processes, operations, style of work, or apparatus, or to the identity, confidential statistical data, amount or source of any income, profits, losses, or expenditures of any person, firm, partnership, corporation, or association.”¹⁰ In addition, the Tax Reform Act establishes confidentiality of tax returns and return information, with few limitations.¹¹

Manufacturers have a long track record of information sharing with the US Food and Drug Administration (FDA) that would be a reasonable model here. With the FDA, a manufacturer can designate part or all the information it provides as proprietary and is therefore exempt from disclosure.¹² Such a designation is made at the time of the data submission or within a reasonable time thereafter. Upon receipt of information designated as confidential, the FDA initiates a regulatorily-defined process for determining whether the information, indeed, falls within an exemption.¹³

Whereas information in the hands of FDA tends to be clinical in nature, and more likely to become public over the normal course of a drug’s patented lifecycle, CMS is requesting detailed, research, operational and sales data that have never been requested or publicized. For example, under R&D expenses, CMS mentions personnel expenses (compensation), which is proprietary.

⁹ Seshamani M. *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments*. Memorandum to Interested Parties. March 15, 2023. (see page 29).

¹⁰ 18 U.S.C. § 1905 (2023) Accessed March 31, 2023 at: <https://www.law.cornell.edu/uscode/text/18/1905>

¹¹ 26 U.S.C. § 6103 (2023) Accessed March 31, 2023 at: <https://www.law.cornell.edu/uscode/text/26/6103>

¹² 21 C.F.R. 20.61. Accessed March 27, 2023 at: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=20.61>

¹³ 21 C.F.R. 20.61. Accessed March 27, 2023 at: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=20.61>

Unit costs of production and distribution would not be the type of information that FDA requests, but it goes to the very heart of business strategy and cost allocations and would never be appropriate for public release. In some cases, the public release of information could violate a manufacturer's agreement with a supplier, such as the price paid for raw ingredients or contracted packaging and shipping costs.

Should CMS decide to proceed with the guidance as drafted, we would raise an additional concern about the lack of protections for some of the data in non-proprietary categories identified by CMS, such as tax credit information included in the definition of prior Federal funding. This information is not public per the Tax Reform Act. Unless CMS can find it lawfully published or made publicly available, it should be protected from public release.

IV. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026: Data Use Provisions and Limitations (40.2.2)

We understand CMS is proposing requirements on Primary Manufacturers pertaining to the submission of data and the use, disclosure, and destruction of data and other information received during the negotiation process. The fact that CMS intends to require a Primary Manufacturer to agree to the terms set forth in the agreement regarding these provisions further bolsters the need to share a draft of the agreement as part of this process with ample opportunity to review and provide feedback to CMS. Anything short of this becomes an accept without change or reject approach that fails to maintain any remnant of a voluntary negotiation.

The approach currently proposed is largely one-sided in which CMS would be allowed to disclose certain data shared as part of the process (section 40.2.1), but the manufacturer would not be allowed to respond based on information considered during the discussions of the set price. On the contrary, if erroneous information is disclosed by CMS as part of its required statement of justification for the maximum fair price (MFP), the manufacturer should be allowed to clarify, for the record, a different point of view on the negotiation. While it is not likely in the best interests of the manufacturer to disclose specifics of prices considered in the negotiation, the ability to share appropriate information, or to correct the record, particularly about justifications should be allowed.

In addition, we are concerned about a requirement to destroy all data within 30 days of a determination by CMS that a drug or biologic no longer qualifies as a selected drug. On the surface, this potentially limits a manufacturer's ability to retain records that to the best of our knowledge may be subject to a legal proceeding or is needed for further internal consideration of future negotiations to which the company may be a part.

We recommend that CMS clarify that the exception to the 30-day destruction rule for state and federal law requirements also encompasses information that may be retained in response to or anticipation of judicial proceedings. Furthermore, we note that the destruction requirement also impairs the retention of institutional knowledge about the rationale for company decisions to be considered in the context of future investments in our ongoing operations.

As a practical matter, it will be difficult for a manufacturer to faithfully produce a “Certificate of Destruction.” The broad and complex scope of modern business communication and the way such communication is internally retained makes it nearly impossible to certify that everything has been destroyed in such a short timeframe (i.e., 30 days). In the case of holding Secondary Manufacturers accountable, if applicable, it is even more difficult.

Finally, we regard these requirements to remain silent in response to disclosures from CMS, while destroying all evidence that may assist in a forensic review of the record, as clearly prejudicial against a manufacturer.

Thus, we believe these provisions need to be revised to address the concerns as described.

V. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026: Providing Access to the MFP (40.4)

In this section, CMS lays out requirements for manufacturers to ensure the MFP for a selected drug is available to pharmacies, mail order services, and other dispensers with respect to MFP-eligible individuals under Part D. We also understand that Part D plan sponsors will ultimately need to ensure MFP-eligible individuals will receive access to the MFP at the point of sale as a basis for cost sharing.

14-Day Reimbursement: Of note is the requirement that the Primary Manufacturer be responsible for ensuring the entities are reimbursed in a timely manner for the differential between their acquisition cost for the selected drug and the MFP within 14 days in the case of the use of a retrospective reimbursement approach. We believe the use of a retrospective reimbursement approach is the preferred mechanism to prevent diversion of Medicare prices to non-eligible individuals. We also question the timing of access to the MFP to occur within 14 days, as written. We expect the process to be incredibly challenging, regardless of the approach. However, the 14-day deadline may be achievable if the deadline occurs after the claim is verified and adjudicated as a “clean claim” prior to adjusting the payment. Any other approach would essentially be impossible, therein shutting down the retrospective option, opening diversion risk under a prospective approach.

We believe that the method currently used to operate the Medicare Part D coverage gap (created under provisions implementing the Patient Protection and Affordable Care Act (ACA) in March 2010) is an effective model that CMS could use in this instance for manufacturers using a retrospective system for implementation.¹⁴ Palmetto GBA serves as a third-party administrator under the program, and has been in that role meeting the requirements under the ACA,¹⁵ since the beginning of the Part D program.

¹⁴ Social Security Act § 1860D-14A. Accessed March 31, 2023 at: https://www.ssa.gov/OP_Home/ssact/title18/1860D-14A.htm

¹⁵ Social Security Act § 1860D-14A(d). Accessed March 31, 2023 at: https://www.ssa.gov/OP_Home/ssact/title18/1860D-14A.htm

Under the approach, the pharmacy claim is processed while a Part D patient is in the coverage gap without any interference to the patient's experience with the program. The manufacturer's coverage gap discount is applied to the pharmacy's reimbursement by the plan sponsor. As described in a Technical Guide from CMS on the Coverage Gap Discount Program (CGDP), the following process keeps all stakeholders whole in the process:¹⁶

- CMS makes prospective payments to Part D Sponsors, enabling them to extend the coverage gap discounts to their beneficiaries at the POS.
- On a quarterly basis, Invoice Reports containing coverage gap PDE data are generated and distributed to Drug Manufacturers and Part D Sponsors via the CGDP Direct Payment Process (DPP) Portal.
- Drug Manufacturers then make payments to Part D Sponsors for the invoiced coverage gap PDE amounts. If applicable, Part D Sponsors also reimburse Drug Manufacturers for any negative amounts invoiced as a result of adjusted or deleted PDEs that were previously invoiced to a Drug Manufacturer.
- On a quarterly basis, CMS offsets subsequent prospective payments to Part D Sponsors by the amount invoiced to Drug Manufacturers.

We believe this approach serves as a model for the implementation of the process for making the MFP available as required under the IRA.

Under our current chargeback systems, payment adjustments typically take at least 14 days to complete with wholesalers and distributors. In that instance, we have full verification of the wholesalers' or distributors' claims being made against the sales. However, reconciliation at the retail level brings the process to a whole new level of complexity. Similarly, section 1927(b)(1)(A) of the Social Security Act (the Act) and the terms of the National Medicaid Drug Rebate Agreement, require manufacturers to pay a rebate to each state within 30 days of the manufacturer's receipt of the state invoice.

Currently, wholesalers process chargebacks that apply to all the manufacturers' sales of the contracted customer. The entire chargeback processing infrastructure is fully automated with very limited human intervention. This allows for a 14-day processing that would cover the process of claims submission, verification, chargeback approval, and subsequent transmission. However, under the MFP the price is owed on each individual eligible purchase. Retail pharmacies do not currently have the system infrastructure to allow fully automated chargeback processing. And wholesalers currently do not have access to data allowing the processing of claims-level chargebacks. A 14-day completion of the payment process is practically impossible without extensive build out of system infrastructures. Pharmacies would need to begin reporting claims-level data to wholesalers electronically in a fully automated system, a burdensome new reporting requirement. Wholesalers would need to be given access to portions of Part D Prescription Drug Event (PDE) data to obtain claims-level data necessary to bill manufacturers for chargebacks correctly.

¹⁶ Centers for Medicare & Medicaid Services. *Coverage Gap Discount Program. Technical Guide. Version 1.0.* August 2021. Accessed March 31, 2023 at: https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/Coverage_Gap_Discount_Program_Technical_Guide_08.2021.v1.pdf

Another challenge with the proposal from CMS is a requirement that the MFP be made against an acquisition cost. Validation of such a charge is complex and costly.

The actual acquisition cost (AAC) for an individual prescription is hard to track and is currently unknown to entities outside the pharmacy. Pharmacies typically purchase medicines from multiple wholesalers at different prices depending on mark-ups, and the quantity purchased can vary significantly. Individual prescriptions can be comprised of a quantity taken from bottles purchased from different wholesalers at different prices depending on the available inventory at the pharmacy. Because of this, only the dispensing pharmacy would be able to know the AAC for a prescription dispensed to an MFP-eligible beneficiary.

Furthermore, manufacturers have no control over the mark-ups a dispenser may pay as part of the distribution network. Those charges are within the purview of the dispenser and its wholesaler or other distributor based on charges for a service.

We believe the manufacturer discount, based on the MFP, should be a function of the wholesale acquisition cost (WAC), which reflects the list price from the manufacturer. Furthermore, this comprises the drug cost portion of the medication charge and not fees associated with other distribution costs assessed to pharmacies and others.

If implemented as proposed, this has the potential to create an incentive that could increase overall system costs. As proposed, the incentive could be to increase fees on pharmacies with the presumption manufacturers would offset those costs as part of the MFP payment. This creates a potential spillover of these fees to the commercial market, Medicaid, and other non-Medicare programs, for which the fees are applied across the board. Thus, this incentive needs to be eliminated.

Negotiation Factors

VI. Manufacturer-Specific Data: Data Elements and Consideration of Manufacturer-Specific Data (50.1; 60.3.4)

CMS notes that manufacturer-specific data is to be reported by the Primary Manufacturer, including any Secondary Manufacturer data, by October 2, 2023. Key factors to be reported include:

- R&D costs for the selected drug and the extent to which the costs have been recouped;
- Current unit costs of production and distribution of the selected drug;
- Prior Federal financial support for novel discovery and development of a selected drug;
- Data on pending and approved patent applications, exclusivities recognized by the FDA; and
- Market data, revenue and sales data in the United States.

In addition, Appendix C provides additional information about the types of information that will be expected early in the MFP negotiation process.

As this process moves forward, we recommend that CMS not limit the timeframe for submission of data to a one-time-only submission of data. Manufacturers should be allowed an opportunity to provide additional information for consideration by CMS as it becomes available.

Furthermore, we have some questions about some of the information to be considered. In addition, it should be recognized that some information will be difficult to provide under the deadline sought.

Research and Development Costs: The challenges for provision of data are especially important as it pertains to research and development (R&D) costs. A submission of this type raises multiple questions as to how to account for the R&D costs for a specific drug and other drugs over time. Furthermore, we are concerned about the lack of scope in what is considered. Thus, while requirements for submission should be limited to specific costs for an individual drug, manufacturers should be given latitude to provide and for CMS to consider other costs related to R&D.

We observe that R&D costs related to new indications or formulations under development but not yet approved seem to be excluded from consideration. However, this is important research in the development of new and existing treatments for patients that may have implications for the use of those treatments. Moreover, to the extent the manufacturer obtains patents related to the development of new indications or formulations, CMS intends to consider adjusting downward the preliminary price. Given the MFP will apply to any new indication or formulation approved after the MFP has been set, those R&D costs, if known at the time, should be considered in the R&D cost calculation. In addition, any adjustments of the preliminary price should also accommodate new R&D costs necessary to the development of the new indications or formulations.

Furthermore, the exclusion of acquisition costs and those pertaining to ongoing basic clinical research, clinical trials and pending approvals from the definition of R&D seems overly simplistic. It is easy to envision a relatively late-stage acquisition of a molecule in which the cost paid to acquire the asset in part reflected pre-acquisition R&D costs. Additionally, many products that reach commercialization were not the initial asset or molecule pursued, but rather reflect learnings from the failures of earlier attempts. The rate at which this occurs is expected to increase with additional exploration of precision and cell and gene therapies. To the extent such costs are knowable, they should not be categorically excluded just because of how and when the costs were borne by the manufacturer, or the ultimate holder of the New Drug Application (NDA) or the Biologics License Application (BLA) holder.

Beyond the descriptors of R&D costs in Appendix C, we believe there should be a further assessment of other identifiable R&D costs as deemed appropriate by the manufacturer. Prior research suggests the complexity of factors that might be important to consider as appropriate

(see “Table 7”).¹⁷ As contemplated in the guidance, only research and development costs associated with a selected drug are used in the evaluation. However, the revenues from the few successful products are utilized to cover the R&D costs across the entire portfolio of medicines, not just those in the same therapeutic class or intended mechanism of action. Of the thousands of potential candidates, only a few may ultimately result in an FDA approved medicine. As such, limiting research and development costs to the selected product only may have the unintended consequence of limiting research to more commercially viable disease states under the IRA’s concept of R&D recoupment. We urge CMS to take a global view of R&D costs and consider additional information that a manufacturer may provide regarding R&D costs.

Table 7.
Impact of total capitalized cost per approved new drug due to changes in individual cost drivers (current study factor effect relative to prior study cost).

Factor Category	Factor
Direct cash outlays	
	Out-of-pocket clinical phase costs
	Pre-human / clinical cost ratio
	Overall out-of-pocket costs
Risk	
	Clinical approval success rate with prior study distribution of failures
	Distribution of failures with prior clinical approval success rate
	Overall risk profile: clinical approval success rate plus distribution of failures
Time	
	Pre-human phase
	Clinical phase
	Regulatory review
	Overall development timeline
Cost of capital	
	Discount rate

Source: DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *Journal of Health Economics*. 2016;47:20-33.

Pending and Approved Patent Applications: The definitions adopted by CMS create considerable confusion about the patent-related data manufacturers must submit. They also require the submission of data that is irrelevant for the purposes of the Negotiation Program. To promote clarity and efficiency, CMS should use terminology and standards for relevance that are consistent with other federal laws and regulations governing the submission of biopharmaceutical patent information to federal agencies, such as 21 CFR 314.53.

Section 1194(e)(1) of the Act specifies that manufacturer-specific data includes “[d]ata on pending and approved patent applications.” CMS considers this to include “all pending and approved patent applications, including expired and non-expired approved patents, submitted, sponsored, licensed, and/or acquired by the Primary Manufacturer relating to the selected drug....” The guidance refers to both “approved patent applications” and “approved patents,” where it is

¹⁷ DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *Journal of Health Economics*. 2016;47:20-33.

apparent Congress intends to mean issued patents. As these terms do not accurately describe issued patents,¹⁸ CMS should simply define “approved patent applications” to mean “patents.”¹⁹

Relevant patents and patent applications include those “relating to the selected drug.” The guidance also describes patents “linked to the selected drug.” It is unclear if CMS intends the phrases to carry different meanings. The guidance is silent on how manufacturers should determine whether patents and patent applications are sufficiently “related to” or “linked to” the selected drug. We request clarification of the standard for relevance of patents and pending patent applications.²⁰

According to the guidance, a “pending patent application” is defined as “any provisional or nonprovisional patent application submitted to the United States Patent and Trademark Office (USPTO) for which a patent number(s) has not been issued.” This definition does not include international applications²¹ designating the United States, which are neither provisional nor nonprovisional applications and which are not necessarily filed with the USPTO. CMS should clarify whether relevant pending patent applications include international applications designating the United States.

The definition of “pending patent application” is also imprecise because it includes abandoned patent applications,²² which are clearly not pending.²³ CMS should clarify that pending patent applications do not include abandoned patent applications.

The definitions of “pending patent application,” “approved patent application,” and “expired patent” all describe the issuance of a patent number as representing a change in status of an application from “pending” to “approved.” It should be noted, however, that patent numbers are not “issued” at the time of patent grant; rather, they are assigned before grant after a fee is paid. The distinction is important because an application may, in fact, have a patent number assigned yet never actually issue as a patent.²⁴ Therefore, assignment of a patent number is not an appropriate indicator that a patent has issued from a patent application.

In addition to lacking clarity, the definitions provided for patent-related data are also overbroad. Under the proposed definitions, manufacturers are required to collect and analyze a significant amount of information about patents and patent applications, including those owned by third parties, which incur considerable time and expense. Given the limited resources we expect

¹⁸ As a technical matter, applications are “allowed” rather than “approved.” *See* 37 CFR 1.311; Manual of Patent Examining Procedure, § 203.04 (9th ed., 2022). Patent applications are also distinct from the patents that issue from them—i.e., an allowed or “approved” patent application is not a patent. *See* 37 CFR 1.314.

¹⁹ The Code of Federal Regulations contains over 2000 references to “patent” or “patent application”; there are zero references to “approved patent application.”

²⁰ The appropriate standard for relevance should be consistent with the purpose for which the data is required. This is discussed in further detail below.

²¹ International applications are commonly filed after a provisional application and become a nonprovisional application only upon entering the national stage in the United States. *See* 37 CFR 1.9(a)(3).

²² Abandoned patent applications have been submitted to the USPTO and have not been assigned a patent number.

²³ *See* 37 CFR 203.05 (“An abandoned application ... is removed from the Office docket of pending applications”)

²⁴ There are various reasons why the USPTO may, after a patent number has been assigned, withdraw an application from issue. *See* 37 CFR 1.313.

will be available to CMS to evaluate this and other manufacturer-specific data, we believe CMS did not intend to require the submission of much of the patent-related data covered by its guidance. Therefore, we ask that the definitions of relevant patents and patent applications include only what is needed to accomplish the purpose for which the data is required.²⁵

For example, the guidance indicated that relevant patent data includes “patents linked to the selected drug where the Primary Manufacturer is not listed as the assignee/applicant (for example, for a joint venture product)” Absent any clarity about what is meant by “linked to,” the proposed definition potentially encompasses numerous third-party patents connected in some way to the selected drug. Third parties routinely obtain patents related to approved drugs covering manufacturing processes, formulations, unapproved uses, different salts or crystalline forms, and combination therapies.²⁶ All of these can be considered to be “linked to” a selected drug.

The required data also includes “all patent applications, pending²⁷ and approved, for which a claim of patent infringement could reasonably be, or has been, asserted against a person engaged in the unlicensed manufacture, use, or sale of the selected drug in any form.” Again, the proposed definition includes patents and patent applications supporting not only claims of infringement by the manufacturer but also claims by third parties.²⁸

Patents and patent applications that are not under the control of the manufacturer by assignment, license, or some contractual obligation should not be considered “Manufacturer-specific data” under Section 1194(e)(1) of the Act. The manufacturer only has data on such third-party patents and patent applications that are already publicly available.²⁹ The guidance also suggests the manufacturer must analyze patents and pending applications for possible claims of infringement. A determination of whether a claim of infringement is reasonable requires information relevant to enforceability. The manufacturer would not have access to this information for third-party patents. The manufacturer must also consider infringement of the selected drug “in any form.” Performing such an extensive analysis for all third-party patents and pending patent applications places an undue burden on the manufacturer.³⁰

According to the guidance, CMS intends to use the data on patents and pending patent applications “to consider the length of the available patents ... before the selected drug may no

²⁵ See Section 60.3.4, Consideration of Manufacturer-Specific Data.

²⁶ For example, as of April 3, 2023, there are 183 granted patents not assigned to Merck that reference the drug sitagliptin by name in their claims. This number does not include patents that reference the drug by chemical name, structure, class, or functional language.

²⁷ Strictly speaking, there can be no infringement of a pending patent application, only issued patents. See 35 U.S.C. 271 § (2023). The claims of pending applications are routinely amended during examination, and applications are frequently abandoned. Therefore, it would be premature for CMS to make determinations about the exclusionary effect of a pending application until it issues as a patent.

²⁸ In addition to the 183 granted patents mentioned in footnote 26, as of April 3, 2023, there are 593 published patent applications that refer to sitagliptin in their claims.

²⁹ Data regarding provisional and unpublished patent applications for which a claim of infringement could reasonably be asserted may not be publicly available because under federal law the applications are kept in confidence by the USPTO. 35 U.S.C. § 122 (2023).

³⁰ One estimate places the cost of performing an infringement opinion at \$7,500 to \$25,000 or more for one patent. Brown & Michaels Budget Estimator for Patents, Brown & Michaels, PC. Accessed April 3, 2023 at: <https://www.bpmlegal.com/content/patfees>.

longer be single source.”³¹ Yet much of the patent-related information the manufacturer is required to submit is irrelevant to this consideration. For example, abandoned patent applications and expired patents can have no effect on a selected drug’s length of exclusivity. Likewise, third-party patents and applications for which the manufacturer has no control over enforcement cannot be used to maintain exclusivity in the market. Many types of patents related to pharmaceutical products are unlikely to prevent generic and biosimilar competition. These include patents covering manufacturing processes and intermediates, different polymorphs and other forms of the active ingredient, metabolites, unapproved uses, and different formulations and dosage forms, which have been deemed by Congress and FDA to not be worthy of listing in the Orange Book and cannot give rise to a 30-month stay of generic approval.³²

New definitions of relevant patent data are unnecessary for the purposes of the Negotiation Program. There already exist standards for the submission of patent-related information to FDA that have been developed from over 20 years of experience. Manufacturers are required to provide such information for listing under section 351(k)(9) of the Public Health Service Act and section §505(j)(7) of the Federal Food, Drug, and Cosmetic Act.³³ CMS should adopt the definitions for relevant patents associated with these requirements. Doing so will improve predictability in the Negotiation Program and minimize the significant burden to manufacturers and CMS of collecting and analyzing irrelevant data. Alternatively, CMS may rely upon the information already submitted by manufacturers found in the Orange and Purple Books. Manufacturers need only supplement the information already available to CMS with data about pending patent applications.

In considering data on patents and regulatory exclusivities, the guidance suggests “if the selected drug has patents and exclusivities that will last for a number of years, CMS may

³¹ Section 60.3.4 (Consideration of Manufacturer-Specific Data).

³² See 68 FR 36676 (June 18, 2003), Final Rule, Food and Drug Administration. “Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed.”

³³ See 42 U.S.C. § 262(l)(3)(A):

(i) a list of patents for which the reference product sponsor believes a claim of patent infringement could reasonably be asserted by the reference product sponsor, or by a patent owner that has granted an exclusive license to the reference product sponsor with respect to the reference product, if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application; ...

and 21 C.F.R. 314.53(b)(1):

An applicant described in paragraph (a) of this section must submit to its NDA the required information, on the required FDA declaration form, set forth in paragraph (c) of this section for each patent that claims the drug or a method of using the drug that is the subject of the NDA or amendment or supplement to it and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. For purposes of this part, such patents consist of drug substance (active ingredient) patents, drug product (formulation and composition) patents, and method-of-use patents For patents that claim a drug product, the applicant must submit information only on those patents that claim the drug product, as is defined in § 314.3, that is described in the pending or approved NDA. For patents that claim a method of use, the applicant must submit information only on those patents that claim indications or other conditions of use for which approval is sought or has been granted in the NDA.

consider adjusting the preliminary price downward.”³⁴ We strongly urge CMS to reconsider and reject this proposal. An approach that penalizes manufacturers for successful innovation would be truly extraordinary. Patents are awarded for inventions that are new, useful, and nonobvious “[t]o promote the Progress of Science and useful Arts.”³⁵ Congress has sought to correct distortions and inefficiencies in pharmaceutical research and development through incentives that *extend* patent term.³⁶ Experience has shown this legislation to be vital to the development and use of safe and effective drugs.³⁷ Adjusting preliminary price downward because there is patent term remaining conflicts with the congressional intent behind these statutory mechanisms. Patents and term extensions awarded to manufacturers are the fruits of innovation and lifesaving research. To penalize manufacturers for obtaining them is to disincentivize this important work.

Second, any attempt to determine the ability of patents to maintain exclusivity often includes a high degree of uncertainty.³⁸ It necessarily includes drawing conclusions about the ability of third parties to avoid or “design around” what is protected by patent. Both technological and regulatory factors are relevant. A generic or biosimilar applicant that has received FDA approval may still launch “at-risk” even if there are patents remaining.³⁹ Opinions of counsel, benefiting from access to a manufacturer’s information and personnel and the investment of hundreds of hours of research and analysis, are still often full of assumptions and caveats. The reality is that biopharmaceutical patent litigation involves considerable uncertainty and risk. In part for this reason, most litigations involving ANDAs are resolved by a settlement between the parties.⁴⁰

For these reasons, it would be inappropriate to use remaining patent term as a justification to penalize manufacturers. In fact, CMS should consider adjusting a preliminary price upward if data about patents and pending patent applications demonstrate innovation that should be encouraged, similar to considerations about whether the selected drug fills an unmet medical need.

Regulatory Exclusivities: Similar to the patent-related incentives discussed above, Congress has frequently used regulatory exclusivities recognized by FDA to incentivize research

³⁴ Section 60.3.4 (Consideration of Manufacturer-Specific Data).

³⁵ U.S. Const. art. I, § 8, cl. 8; 35 U.S.C. §§ 101, 102, 103 (2023).

³⁶ *See, e.g.*, 35 U.S.C. § 156 (extending the term of patents covering approved drug products to compensate for term lost during regulatory review); 21 U.S.C. § 355a(b)(1)(B) (extending the term of patents listed in the Orange Book by six months in return for conducting pediatric studies).

³⁷ *See, e.g.*, U.S. Food and Drug Administration. *The Pediatric Exclusivity Provision, January 2001 Status Report to Congress*. Accessed April 3, 2023 at: <https://www.fda.gov/media/99580/download> (“The pediatric exclusivity provision has done more to generate clinical studies and useful prescribing information for the pediatric population than any other regulatory or legislative process to date.”)

³⁸ This uncertainty is even more true of pending patent applications. As described above, the claims of pending applications are almost always amended during examination and applications frequently are abandoned for various reasons. Therefore, it would be particularly improper for CMS to rely on pending patent applications to adjust a preliminary price downward.

³⁹ *See* Drake, KM et al. No Free Launch: At-risk Entry by Generic Drug Firms. NBER Working Paper No. 29131, August 2021. National Bureau of Economic Research. Available at: https://www.nber.org/system/files/working_papers/w29131/w29131.pdf.

⁴⁰ *See* Swaroop, S et al. Recent Trends in ANDA Litigation. pharmaphorum.com (December 19, 2016) Accessed April 10, 2023 at <https://pharmaphorum.com/views-and-analysis/recent-trends-anda-litigation> (finding that nearly 60% of ANDA result in a settlement).

and development. These include exclusivities associated with orphan drugs, qualified infectious disease products, new clinical studies, and pediatric studies. Penalizing a manufacturer for succeeding in this research would be antithetical to these statutory incentives and section 1194(e)(2) of the Act, which requires CMS to consider evidence about the extent to which the selected drug addresses unmet medical needs and treats specific populations, including children.

Net Price Calculation: There are several places where measures, such as rebates, discounts, and chargebacks, appear to be excluded from net price or revenue calculations. We agree this is important but note there does not appear to be a consideration of distribution costs, such as fees and other charges paid to pharmacy benefit managers (PBMs), group purchasing organizations (GPOs) or other entities that add to distribution costs, thus influencing the net cost of the medication. We believe these costs need to be considered as well.

We also note that guidance seems to require global revenues be used in pricing calculations, but expenses and other discounts to be considered are US centric. This results in an apples to oranges calculation that disadvantages the manufacturer. If CMS adopts a global revenue number, the global discounts and expenses need to be reflected fully as well.

Adding to the overall costs manufacturers face, but excluded from the guidance currently, are government compliance and coverage-related evidence generation costs. There is precedent for considering compliance costs elsewhere in government programs. For example, this approach was used in the treatment of the health insurer tax in health plan medical loss ratio calculations. We believe options for a fair approach to this issue in the MFP context would be to subtract the costs from revenues or via an addition to the costs of production and distribution. Since global sales are being considered in the revenue definition, it seems appropriate that the cost of generating evidence to get coverage in other countries should, likewise be included in the assessment.

Certainly, the defining unit costs are complex, inclusive of investments at many levels across the research, development, and production process. If CMS is committed to weighting input costs in its negotiation process, it is important that manufacturers be given an opportunity to fully represent their costs, including costs that CMS might not have envisioned.

Tax Credits: Inclusion of tax credits in the definition of federal financial support is concerning to us. First, tax returns and information are confidential under the Tax Reform Act and should not be requested by CMS. Additionally, these credits exist for public policy reasons. Congress wanted to incentivize behaviors that drive innovation for manufacturing in the United States. Conversely, if tax information is going to be used as a rationale to drive down CMS's offered prices (thus, inflating the federal support factor), tax payments of all types (global, U.S., tariffs, state and local, user fees, the ACA industry fee) clearly are operational costs and should be deducted from any revenue calculation.

VII. Manufacturer-Specific Data: Evidence About Therapeutic Alternatives for the Selected Drug (50.2)

The guidance lays out a series of critical issues essential to the process of considering medications and alternatives to treatments that may be subject to the establishment of a price by CMS and those that may be considered an alternative treatment. In the evaluation by CMS, it intends to:

- Consider whether a selected product represents a therapeutic advance compared to the therapeutic alternatives;
- Evaluate FDA-approved prescribing information among comparable products;
- Consider comparative effectiveness research, inclusive the of the implications for “specific populations”; and
- Assess the extent to which a treatment addresses an unmet medical need.

Therapeutic Alternatives: To identify potential therapeutic alternatives for the indications of a selected drug, CMS intends to use data submitted by the Primary Manufacturer and the public, FDA-approved indications, indications included in CMS-approved Part D compendia, widely-accepted clinical guidelines, and peer-reviewed studies. However, a key question for this section pertains to what constitutes a therapeutic alternative. Without this definition, the comparisons sought are not possible. How therapeutic alternatives are defined tends to vary by payer and is neither readily available nor standardized. It is primarily a function of drug reviews conducted by the pharmacy and therapeutics (P&T) committee of a plan or other drug management entity, inclusive of the opinions of the members and support staff of the committees. Much of this information is kept from public view.

Often, when these types of considerations are made, it is implicit that the medications could be easily substituted for one another via therapeutic interchange. However, this is not generally supported without the prescribing practitioner’s approval or collaborative protocols. Statements espousing that position include those from the Academy of Managed Care Pharmacy (AMCP),⁴¹ the National Association of Boards of Pharmacy (NABP),⁴² American College of Cardiology Foundation,⁴³ and the American Medical Association (AMA).⁴⁴

The approach being discussed is not a matter of switching, although the ultimate impact may be to influence access to certain medications, via some form of interchange or financial incentives to patients. Hence, in considering supposed therapeutic alternatives, an approach for

⁴¹ AMCP. *Therapeutic Interchange*. June 1, 2019. Accessed March 28, 2023 at: <https://www.amcp.org/policy-advocacy/policy-advocacy-focus-areas/where-we-stand-position-statements/therapeutic-interchange-0>

⁴² National Association of Boards of Pharmacy. *Report of the Task Force on Therapeutic Interchange*. Accessed March 28, 2023 at: https://nabp.pharmacy/wp-content/uploads/2016/07/TF_Therapeutic_Interchange.pdf

⁴³ Holmes DR, Becker JA, Granger CB, et al. ACCF/AHA 2011 Health policy statement on therapeutic interchange and substitution. *Circulation*. 2011;124:1290-1310.

⁴⁴ American Medical Association. *Drug Formulary and Therapeutic Interchange H-125.991*. Year Last Modified: 2020. Accessed March 28, 2023 at: <https://policysearch.ama-assn.org/policyfinder/detail/Drug%20Formularies%20and%20Therapeutic%20Interchange%20H-125.991?uri=%2FAMADoc%2FHOD.xml-0-227.xml>

CMS' consideration of the term is a definition used by the American Society of Health System Pharmacists set forth as follows:⁴⁵

Therapeutic Alternatives. Drug products with different chemical structures but of the same pharmacologic or therapeutic class and usually have similar therapeutic effects and adverse-reaction profiles when administered to patients in therapeutically equivalent doses.

Certainly, clinically appropriate comparisons are essential. Furthermore, there are multiple publications that differentiate medications, grouping them in a manner that attempts to meet this definition. These publications include, but are not limited to the *American Hospital Formulary Service (AHFS) Drug Information*, and the *United States Pharmacopeia-Drug Information*. However, differences exist among publications and the classification approach. In practice, there are reasons why one grouping may be more appropriate than another, depending on the application.

Another consideration beyond the definition of “therapeutic alternative” would be the clinical appropriateness of the alternative, as directed by guidelines, compendia, and other evidence-based research. We strongly encourage CMS to incorporate clinician guidance as well as evidence-based guidelines as part of the qualifying documentation to drive its decision-making process regarding therapeutic alternatives.

Irrespective of the initial approach used, we believe that the identification of therapeutic alternatives must be done by CMS in a public manner that allows for comments from the manufacturer and other key stakeholders. This should consider both clinical and non-clinical benefits for patients. Furthermore, we believe manufacturers of selected products be allowed to offer their recommended grouping of medications, inclusive of the justification for consideration by CMS during the price setting process.

Therapeutic Advance / Unmet Medical Need: The determination of a therapeutic advance depends on the perspective of who is making the determination and can mean different things to different people. There are currently different approaches in existence that are well known. Following are three examples which should serve as a starting point for consideration.

Food and Drug Administration: The FDA sets forth important criteria for the determination of fast-track approvals, breakthrough therapy, accelerated approval and priority reviews.⁴⁶ As described by FDA, the high-level standards include the following:

- **Fast Track:** Fast track is a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need.

⁴⁵ Sanders GD, Neumann PJ, Basu A, et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses. Second panel on cost-effectiveness in health and medicine. *JAMA*. 2016;316(10):1093-1103.

⁴⁶ U.S. Food and Drug Administration. *Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review*. Content current as of February 23, 2018. Accessed March 28, 2023 at: <https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review>

- Breakthrough Therapy: A process designed to expedite the development and review of drugs which may demonstrate substantial improvement over available therapy.
- Accelerated Approval: These regulations allowed drugs for serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint.
- Priority Review: A Priority Review designation means FDA's goal is to take action on an application within 6 months.

We believe each of these FDA designations represent a minimum standard for a therapeutic advance. However, this should not be the only basis for such a designation.

For example, newer medications in a treatment class may offer critical advances in therapy regarding the adverse event profile, ease of administration (e.g., oral versus intravenous) or impact on a patient's quality of life or overall survival. All of these must be considered in the evaluation of a therapeutic advance.

Specifically, concerning the determination of an unmet medical need, we reference the FDA guidance document further addressing expedited programs. In this document, the definition of an unmet medical need is as follows:⁴⁷

An unmet medical need is a condition whose treatment or diagnosis is not addressed adequately by available therapy. An unmet medical need includes an immediate need for a defined population (i.e., to treat a serious condition with no or limited treatment) or a longer-term need for society (e.g., to address the development of resistance to antibacterial drugs).

1. Where There Is No Available Therapy

If there is no available therapy for a serious condition, there is clearly an unmet medical need.

2. Where There Is Available Therapy

When available therapy exists for a condition, a new treatment generally would be considered to address an unmet medical need if the treatment:

- Has an effect on a serious outcome of the condition that is not known to be influenced by available therapy (e.g., progressive disability or disease progression when the available therapy has shown an effect on symptoms, but has not shown an effect on progressive disability or disease progression)
- Has an improved effect on a serious outcome(s) of the condition compared with available therapy (e.g., superiority of the new drug to available therapy when either used alone or in combination with available therapy (i.e., as demonstrated in an add-on study))
- Has an effect on a serious outcome of the condition in patients who are unable to tolerate or failed to respond to available therapy
- Can be used effectively with other critical agents that cannot be combined with available therapy
- Provides efficacy comparable to those of available therapy, while (1) avoiding serious toxicity that occurs with available therapy, (2) avoiding less serious toxicity that is common and causes discontinuation of treatment of a serious condition, or (3) reducing the potential for harmful drug interactions

⁴⁷ US Department of Health and Human Services. Food and Drug Administration. Center for Drug Evaluation and Research (CDER). Center for Biologics Evaluation and Research (CBER). *Guidance for Industry – Expedited Programs for Serious Conditions – Drugs and Biologics*. May 2014 – Procedural. OMB Control No. 0910-0765.

- Provides safety and efficacy comparable to those of available therapy but has a documented benefit, such as improved compliance, that is expected to lead to an improvement in serious outcomes
- Addresses an emerging or anticipated public health need, such as a drug shortage.

In some disease settings, a drug that is not shown to provide a direct efficacy or safety advantage over available therapy may nonetheless provide an advantage that would be of sufficient public health benefit to qualify as meeting an unmet medical need. For example, in a condition for which there are approved therapies that have a modest response rate or significant heterogeneity in response, a drug with a novel mechanism of action (but comparable safety and effectiveness) could have the potential to provide an advantage over available therapy in some patients. In such a case, the novel mechanism of action should have a well-understood relationship to the disease pathophysiology. In addition, there should be a reasonable basis for concluding that a significant number of patients may respond differently to the new drug compared with available therapy. Thus, mechanistic diversity, even without a documented efficacy or safety advantage, could be advantageous in disease settings in which drugs become less effective or ineffective over time.

For example, infectious disease drugs or targeted cancer therapies with novel mechanisms of action, although appearing to have efficacy similar to available therapy across the disease population, could benefit patients who no longer respond to available therapy. Accordingly, FDA intends to consider a range of potential advantages over available therapy beyond those shown in head-to-head comparisons.

3. Where the Only Available Therapy Was Approved Under the Accelerated Approval Program Based on a Surrogate Endpoint or an Intermediate Clinical Endpoint and Clinical Benefit Has Not Yet Been Verified

As discussed in sections VII and III.B., FDA recognizes, as a general matter, that it is preferable to have more than one treatment approved under the accelerated approval provisions because of the possibility that clinical benefit may not be verified in postapproval confirmatory trials. FDA will therefore consider products as addressing an unmet medical need if the only approved treatments were granted accelerated approval based on a surrogate endpoint or an intermediate clinical endpoint and clinical benefit has not been verified by post approval studies.

With this FDA definition as a starting place, we believe the definition needs to be broadened for purposes of what else should be considered by CMS as an unmet medical need.

New Technology Add-on Payment (NTAP): The Medicare Inpatient Prospective Payment System (IPPS) includes an approach for a new “add-on payment” for “new technologies” known as the NTAP.⁴⁸ This may present another set of considerations for the determination of a therapeutic advance or achieving an unmet medical need. As noted in the related regulations, the medical service or technology must demonstrate a substantial clinical improvement over new technology.

⁴⁸ Centers for Medicare and Medicaid Services. *New Medical Services and New Technologies: Overview of the New Technology Add-on Payment*. Accessed March 30, 2023 at: <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/newtech>

CMS describes the criteria for such a “substantial clinical improvement” as follows:⁴⁹

To qualify for a new technology add-on payment, the technology must represent an advance that substantially improves, relative to technologies previously available, the diagnosis or treatment of Medicare beneficiaries. CMS assesses the following in its evaluation of whether a technology meets the substantial clinical improvement criterion for the purposes of the NTAP:

1. The new technology offers a treatment option for a patient population unresponsive to, or ineligible for, currently available treatments.
2. The new technology offers the ability to diagnose a medical condition in a patient population where that medical condition is currently undetectable or offers the ability to diagnose a medical condition earlier in a patient population than allowed by currently available methods. There must also be evidence that the use of the new medical service or technology to make a diagnosis affects the management of the patient.
3. The use of the new medical service or technology significantly improves clinical outcomes relative to services or technologies previously available.

Specifically, the eligibility criteria are as follows:⁵⁰

Eligibility criteria. For discharges occurring on or after October 1, 2001, CMS provides for additional payments (as specified in § 412.88) beyond the standard DRG payments and outlier payments to a hospital for discharges involving covered inpatient hospital services that are new medical services and technologies, if the following conditions are met:

- (1) A new medical service or technology represents an advance that substantially improves, relative to technologies previously available, the diagnosis or treatment of Medicare beneficiaries.
 - (i) The totality of the circumstances is considered when making a determination that a new medical service or technology represents an advance that substantially improves, relative to services or technologies previously available, the diagnosis or treatment of Medicare beneficiaries.
 - (ii) A determination that a new medical service or technology represents an advance that substantially improves, relative to services or technologies previously available, the diagnosis or treatment of Medicare beneficiaries means one of the following:
 - (A) The new medical service or technology offers a treatment option for a patient population unresponsive to, or ineligible for, currently available treatments.
 - (B) The new medical service or technology offers the ability to diagnose a medical condition in a patient population where that medical condition is currently undetectable, or offers the ability to diagnose a medical condition earlier in a patient population than allowed by currently available methods and there must also be evidence that use of the new medical service or technology to make a diagnosis affects the management of the patient.
 - (C) The use of the new medical service or technology significantly improves clinical outcomes relative to services or technologies previously available as demonstrated by one or more of the outcomes described in paragraphs (b)(1)(ii)(C)(I) through (7) of this section.
 - (1) A reduction in at least one clinically significant adverse event, including a reduction in mortality or a clinically significant complication.
 - (2) A decreased rate of at least one subsequent diagnostic or therapeutic intervention.
 - (3) A decreased number of future hospitalizations or physician visits.
 - (4) A more rapid beneficial resolution of the disease process treatment including, but not limited to, a reduced length of stay or recovery time

⁴⁹ Centers for Medicare and Medicaid Services. *New Medical Services and New Technologies: Overview of the New Technology Add-on Payment*. Accessed March 30, 2023 at: <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/newtech>

⁵⁰ 42 C.F.R. 412.87 (b) Accessed March 30, 2023 at: <https://www.ecfr.gov/current/title-42/chapter-IV/subchapter-B/part-412/subpart-F/subject-group-ECFR5703923263fedba/section-412.87>

- (5) An improvement in one or more activities of daily living
- (6) An improved quality of life
- (7) A demonstrated greater medication adherence or compliance.
- (D) The totality of the information otherwise demonstrates that the new medical service or technology substantially improves, relative to technologies previously available, the diagnosis or treatment of Medicare beneficiaries.
- (iii) Evidence from published or unpublished information sources from within the United States or elsewhere may be sufficient to establish that a new medical service or technology represents an advance that substantially improves, relative to services or technologies previously available, the diagnosis or treatment of Medicare beneficiaries. Information source may include the following:
 - (A) Clinical trials;
 - (B) Peer reviewed journal articles;
 - (C) Study results;
 - (D) Meta-analyses;
 - (E) Consensus statements;
 - (F) White papers;
 - (G) Patient surveys;
 - (H) Case studies;
 - (I) Reports;
 - (J) Systematic literature reviews;
 - (K) Letters from major healthcare associations;
 - (L) Editorials and letters to the editor; and,
 - (M) Public comments.
 - (N) Other appropriate information sources may be considered.
- (iv) The medical condition diagnosed or treated by the new medical service or technology may have a low prevalence among Medicare beneficiaries.
- (v) The new medical service or technology may represent an advance that substantially improves, relative to services or technologies previously available, the diagnosis or treatment of a subpopulation of patients with the medical condition diagnosed or treated by the new medical service or technology.

NCCN Guidelines: The National Comprehensive Cancer Network (NCCN) utilizes a distinct process for the evaluation and development of recommendations for interventions to prevent, diagnose and manage cancers at their different stages.⁵¹ The approach uses a careful analysis of available evidence about various treatments for cancer and preferences for approaches to treatments. As part of the process, the quality of the evidence and the consensus of panels reviewing the evidence come together to assess the level of appropriateness for a treatment for a specific type of cancer.

For example, the highest NCCN rating among four levels is Category 1, which is granted to those for which there is high-level evidence and a uniform NCCN consensus on the appropriateness of the intervention.⁵² The next level – Category 2A – represents treatments, based on lower-level evidence, that have a uniform NCCN consensus based on appropriateness of the intervention. These two categories must reach an 85% majority support among the panelists for a treatment to achieve one of these ratings. Furthermore, NCCN includes categories of preference

⁵¹ National Comprehensive Cancer Network. *Development and Update of Guidelines*. Accessed May 31, 2023 at: <https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines>

⁵² National Comprehensive Cancer Network. *Development and Update of Guidelines*. Accessed May 31, 2023 at: <https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines>

in their reviews. The three categories are: 1) Preferred intervention; 2) Other recommended intervention; and 3) Useful in certain circumstances.⁵³

These evaluations give a sense of medical need in the oncology space for medications and their appropriateness in the treatment of specific cancer variations. Thus, CMS should consider these evaluations further as a basis for consideration of significant therapeutic advance and unmet medical need.

Therapeutic Advance / Unmet Medical Need Summation: Each of these assessments represent examples of important evaluations that influence the use and access to treatments for patients. They serve as a minimal basis for measures of assessing a therapeutic advance or unmet medical need. However, these should not be the only factors CMS considers in this regard. Other considerations should include items, such as the removal or reduction of a significant adverse event that may be related to other alternative treatments, or advances the ability for patients to remain out of a hospital or other institution, thereby helping to reduce health system costs while improving patient quality of life. Furthermore, factors pertaining to improvements in care for disadvantaged groups and overcoming health disparities should be considered.

This is a starting point from which CMS needs to take a longer view when deciding the price for a medication in the Medicare program.

Negotiations

VIII. MFP Ceiling Price (60.2)

Overall, there are at least two main scenarios for which we believe the ceiling price should be set at a level at the maximum ceiling price. Our perspectives follow.

Newer Medications: As the IRA rolls out, small molecule drugs will potentially face price determinations being applied as soon as 9 years after approval. In the case of a biologic, price determinations would not be applied before 13 years. This short timeline for small molecules creates a significant and disproportionate disincentive for manufacturers to continue to develop new indications for a treatment being brought to market.

In our experience, all indications are not submitted for approval immediately. Often, the approach is to bring new treatment options to the market as quickly as possible, such as those for cancer. The delays for certain indications are often beyond the manufacturers' control. Contributing factors such as the available number of trial participants for a trial in question, the time it takes to recruit patients, the time to ensure appropriate regulatory agency guidance is incorporated, or available resources to pursue all potential avenues at one time, to name a few. Thus, there have been important new indications we have seen emerge and continue to be sought following the initial approval of a new medication. This may result in a new indication being approved years after the approval of the first indication.

⁵³ National Comprehensive Cancer Network. Development and Update of Guidelines. Accessed May 31, 2023 at: <https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines>

This situation creates a dilemma for manufacturers pursuing multiple indications. On the one hand, the goal is to make a treatment available to patients in need as soon as possible. However, by doing so without pursuing approval for all conceivable indications, the manufacturer would be giving up valuable resources that may be used to invest in ongoing research. As an example, this is particularly important as efforts are undertaken to determine the effectiveness of a particular treatment for other types of cancer for which additional treatments are surely needed. Without that research, critical information on the risk-benefit and appropriate use of a medication may not be available.

To help minimize this situation, we recommend CMS take a stance of maximizing the MFP within the limits of the ceiling price. This approach could be done in a way that maintains that maximum ceiling price at least up until the first 13 years post approval. The approach also would help limit the disadvantage of bringing a small molecule to market versus a biologic. While this approach still raises significant concerns, even within the context of the ceiling price, it at least creates some level of certainty that the set price will not be lower than the ceiling, helping to lower the potential risk assessment.

Significant Therapeutic Advances & Unmet Medical Need: In our prior discussion in this letter pertaining to the identification of therapeutic advances and addressing unmet medical needs, we raised several ways to make a determination of these advances.⁵⁴

To recount, this includes recommendations from:

- Food and Drug Administration: The FDA sets forth important criteria for the determination of fast-track approvals, breakthrough therapy, accelerated approval and priority reviews.⁵⁵ Designations pertaining to review status may include Fast Track approvals, Breakthrough Therapy designations, Accelerated Approval status, and Priority Review status: We believe each of these FDA designations represent a minimum standard for a therapeutic advance. An unmet medical need is a condition whose treatment or diagnosis is not addressed adequately by available therapy. An unmet medical need includes an immediate need for a defined population (i.e., to treat a serious condition with no or limited treatment) or a longer-term need for society (e.g., to address the development of resistance to antibacterial drugs). When such a status is granted, these medications should receive no lower than the ceiling price.
- New Technology Add-on Payment (NTAP): The Medicare Inpatient Prospective Payment System (IPPS) includes an approach for a new “add-on payment” for “new technologies” known as the NTAP.⁵⁶ For treatments

⁵⁴ See VII. Manufacturer-Specific Data: Evidence About Therapeutic Alternatives for the Selected Drug (50.2)

⁵⁵ U.S. Food and Drug Administration. *Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review*. Content current as of February 23, 2018. Accessed March 28, 2023 at: <https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review>

⁵⁶ Centers for Medicare and Medicaid Services. *New Medical Services and New Technologies: Overview of the New Technology Add-on Payment*. Accessed March 30, 2023 at: <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/newtech>

meeting this standard of achieving a therapeutic advance or achieving an unmet medical need, the medical service or technology must demonstrate a substantial clinical improvement over new technology. Thus, this designation should result in a ceiling price being granted for these treatments.

- **NCCN Guidelines:** The National Comprehensive Cancer Network (NCCN) utilizes a distinct process for the evaluation and development of recommendations for interventions to prevent, diagnose and manage cancers at their different stages.⁵⁷ The approach utilizes a careful analysis of available evidence about various treatments for cancer and preferences for approaches to treatments. As part of the process, the quality of the evidence and the consensus of panels reviewing the evidence come together to assess the level of appropriateness for a treatment for a specific type of cancer. In addition, medications receiving a Category 1 or 2A rating should be granted a price at the ceiling price.

In addition, we encourage CMS to consider additional factors that help achieve other measures of unmet medical need and achieve therapeutic advances beyond these measures, as previously discussed.

Overall, it is our opinion that products that offer significant medical advances and treat unmet medical needs should result in a price that does not drop below the established ceiling price. Factors, among others, should include the engagement of clinicians and the expertise of the manufacturers responsible for the respective medications.

IX. Negotiation Process (60.4)

Meetings Between CMS and Manufacturers: CMS describes a process through which a price will be determined in setting the MFP. Of particular interest is the potential for “up to three possible in-person or virtual negotiation meetings between the Primary Manufacturer and CMS...” One of our concerns pertains to how a meeting is ultimately defined.

We recommend an approach where CMS assigns a level to different types of meetings, with only the highest level being recognized as counting toward the limit established by CMS. The highest-level meeting would be reserved to discuss specific information to support an offer or counteroffer being made in the price-establishment process. At the time of scheduling such a meeting, it should be noted to the manufacturer the level of meeting being set and whether it counts against the limit. Should it be determined there is a disagreement in the level being set, the manufacturer should be granted the option to decline the meeting until such time further discussions are warranted.

We envision other potential meetings as being informational in nature. For example, a request to discuss specific information sought by CMS, clarity on completing forms issued by

⁵⁷ National Comprehensive Cancer Network. *Development and Update of Guidelines*. Accessed May 31, 2023 at: <https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines>

CMS, or clarification on an offer from CMS or the manufacturer, might be considered a lower-level meeting that would not count against the formal process.

The FDA has a more complex approach that helps to serve as a precedent for establishing a similar process by CMS.⁵⁸ As with the FDA guidance, there should be CMS guidance for good meeting management practices (GMMPs) and standardized procedures for requesting, preparing, conducting, and documenting formal meetings. As FDA notes:

Each year, FDA review staff participate in many meetings with requesters who seek advice relating to the development and review of investigational new drugs and biologics, and drug or biological product marketing applications. Because these meetings often represent critical points in the regulatory process, it is important that there are efficient, consistent procedures for the timely and effective conduct of such meetings. The GMMPs in this guidance are intended to provide consistent procedures that will promote well-managed meetings and to ensure that such meetings are scheduled within a reasonable time, conducted efficiently, and documented appropriately.

In a similar manner, key meetings with CMS indicate critical points in the establishment of a price. Thus, standards should be established for these meetings.

Compliance and Penalties

X. Manufacturer Compliance and Oversight (90)

In accordance with section 1196(a)(3)(A) of the Act, CMS intends to establish procedures for reporting violations related to access to the MFP under Part D of title XVIII or MA-PD plan under Part C. CMS would also expect manufacturers and other stakeholders to report instances in which a dispenser was not passing through the MFP to an MFP-eligible individual, or a dispenser was extending the MFP to non-MFP-eligible individuals. CMS is seeking comment on how such a process would operate most effectively, including suggestions on ways that CMS could provide technical assistance to entities to ensure they are able to provide the MFP to MFP-eligible individuals and ways to ensure that MFP-eligible individuals whose cost-sharing was not consistent with MFP are made whole.

We appreciate that CMS is looking to establish a robust and fair process for reporting of violations. We further believe that such a reporting process for potential violations should be developed hand in hand with a robust dispute resolution process for the process to be fair and equitable. CMS should go through a notice and comment rulemaking process to establish such reporting of violations and dispute resolution process similar to the process that was used in establishing the recent 340B Program's dispute resolution process.

Among the issues that must be addressed in establishing a fair violations reporting process are: (1) equal access to the process by all parties; (2) competence and independence of the investigators receiving and acting on the reported violations; (3) clear parameters of what can be reported as violations; (4) defined process for how a report should be received, handled,

⁵⁸ US Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products: Guidance for Industry. (DRAFT GUIDANCE)*. December 2017, Procedural.

communicated, and resolved. As the reported violations may result in non-compliance and potential Civil Monetary Penalties (CMP), a robust dispute resolution process and fair hearing process must be established. We strongly encourage CMS to do this through the notice and comment rulemaking process.

XI. Civil Monetary Penalties (100)

The guidance in Section 100 addresses the Civil Monetary Penalties (CMP) set forth in section 1197 of the SSA (the Program-related CMPs). CMS provided the “procedures” CMS intends to follow to impose these CMPs on manufacturers. We believe that CMS can only implement these CMPs in a manner that conforms to the statute through a notice and comment rulemaking process. ***Section 1197 authorizes extraordinarily high CMP penalties equal to \$100 million for each item of false information and \$1 million per day for failing to provide the information required under section 1193(a)(4) warrant notice-and-comment rulemaking prior to Agency implementation.***

Due to the complexities and many ambiguities that exist in the program, there will be implementation gaps and shortcomings that may potentially cause undue harm to a manufacturer and unfair administration of the determination of a violation and resulting penalties. To safeguard against this, we strongly request CMS to develop the implementation rules for this CMP section through the notice-and-comment rulemaking process before seeking to impose any Program-related CMPs on a manufacturer. The rulemaking process should address the following issues:

- (1) Scope: Specific identification by CMS of violations that would qualify for a Section 1197 CMP and the amounts that correspond to the specific violation;
- (2) Transparency: Detailed procedures for the determination of violations and imposition of the Section 1197 CMPs;
- (3) Review and Appeal Process: Clear process for reviewing and appealing a Section 1197 CMP to provide the manufacturer due process and ensure fairness.

Section 100.4 of the proposed guidance state that CMS will provide manufacturers that violate any of the provisions with a notice regarding the CMP, in accordance with section 1128A of the Act. The notice will include the option to either pay the CMP or to request a hearing as outlined in section 1128A. The CMP notice will include the (1) basis for the CMP; (2) CMP amount due; (3) deadline for the manufacturer to respond with a hearing request or submit the CMP payment; (4) method to submit CMP payment(s); and (5) Information on the right to request a hearing. We believe that a hearing to contest the CMP amount should not be the only recourse of the manufacturer. Prior to sending a CMP Notice, manufacturers should be allowed to appeal the finding of non-compliance and violation. CMP assessments and notifications should be stayed pending result of the appeal. Should an appeal confirm that a manufacturer is in violation of the provisions that warrant CMPs, a final opportunity for a hearing related solely to the CMP, as described by the CMS guidance should be available to the manufacturer.

Non-Compliance by Third Parties Unrelated to Manufacturer: As part of the dispute resolution process, the manufacturer should be able to raise as a defense, that the violation at issue was committed by a third party and not by the manufacturer. We urge CMS to not impose CMPs on drug manufactures for unrelated third-party non-compliance.

We oppose CMS' intention to hold a "Primary Manufacturer" responsible for certain acts and omissions of a "Secondary Manufacturer" or other third parties. The primary manufacturer has no control over the acts and omission of an unrelated third party. Therefore, acts and omissions by an unrelated secondary manufacturer or third party should not be attributed as a violation by the primary manufacturer. We are deeply concerned that CMS, without a proper dispute resolution process, could impose \$1 million-per-day CMPs on a Primary Manufacturer for acts or omissions by third parties unrelated to the primary manufacturer.

In addition, we strongly oppose any interpretation of the statute that would seek to impose CMP liability on manufacturers of selected drugs due to the acts or omissions of any unrelated third party. CMS has proposed to hold Primary Manufacturers ultimately responsible for ensuring access to the MFP. There are many components and entities involved in making a drug's discounted price available to the patient at the time of purchase or through a rebate process. The pharmacy must have the proper infrastructure in place to administer and process a discount and 'chargeback' the MFP discount to a wholesaler or distributor. A wholesaler or distributor must need to have the proper infrastructure in place to process the MFP discount to the appropriate drug manufacturer. The primary manufacturer cannot control how these pharmacies, wholesalers and distributors run their businesses. It would be unfair to attribute all the failures of a supply chain network of these entities to the primary manufacturer.

Knowingly Standard Should be Limited to Actual Knowledge: The guidance uses the "knowingly standard" for determining noncompliance of various requirements. In Section 1197(c) of the SSA, a manufacturer that knowingly submits such information is subject to a CMP equal to \$100 million for each item of false information. In Section 100.2 of the Guidance, CMS states that a manufacturer would be out of compliance if it knowingly submits false information required under the agreement between the manufacturer and CMS and subject to a CMP equal to \$1 million per day of a violation under section 1197(c).

We believe that noncompliance should only occur if the manufacturer has actual knowledge of a violation instead of merely 'knowingly' committed or omitted certain acts that result in a violation. The term 'knowingly' is not defined in section 1128A of the SSA, which is incorporated by reference into the Program-related CMPs. Nor is the term "knowingly" defined in Part E of Title XI of the SSA. There is no legally binding definition of 'knowingly'. The plain meaning of the term 'knowingly' requires one to act "in a way that suggests one has secret knowledge or awareness."⁵⁹ An act that suggests awareness or secret knowledge is not sufficient to establish guilt. Actual awareness and actual knowledge should be established before a liability attaches. ***Given the excessive fines and penalties that may be imposed, we strongly urge CMS to adopt the 'actual knowingly' standards. Such actual knowledge standard eliminates doubt as to the intent and awareness of the party performing the act.***

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⁵⁹ Dictionary, Definitions from Oxford Languages; 'Knowingly', https://www.google.com/search?q=knowingly&rlz=1C1GCEB_enUS1001US1001&oq=knowingly&aqs=chrome..69i57.6865j0j7&sourceid=chrome&ie=UTF-82023). Last visited April 4, 2023.

Again, Bayer appreciates the opportunity to offer these recommendations and hopes to continue its engagement with CMS as the program is implemented.

Sincerely,

A handwritten signature in black ink that reads "Brian Nagle". The signature is written in a cursive, flowing style.

Brian Nagle
Head of U.S. Federal Government Affairs
Healthcare and Policy
Bayer

April 14, 2023

Chiquita Brooks-LaSure
CMS Administrator
7500 Security Boulevard
Baltimore, MD 21244-1850

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director
of the Center for Medicare
7500 Security Boulevard
Baltimore, MD 21244-1850

Dear Ms. Brooks-LaSure and Dr. Seshamani,

Thank you for the opportunity to comment on the initial guidance for implementing the Medicare drug price negotiation provisions of the Inflation Reduction Act.

In considering how to proceed, it would be well to remember the adage: "First, do no harm." While the issue of making drugs more affordable is well outside the scope of the Bayh-Dole Coalition, one factor stood out to us as posing a very real danger to our ability to continue to lead the world in the creation of life-saving therapies. That is the idea that those who commercialize federally-funded inventions have received some sort of advantage that should be used against them when negotiating drug prices. This is a serious fallacy which can do irreparable harm to the most innovative system in the world. And NIH should know this better than most.

Before 1980, the government took inventions away from their creators. When President Johnson asked the Comptroller General why no drugs were created from the billions of taxpayer dollars funding NIH research, the answer was that the incentives needed for the private sector to undertake the tremendous risk and expense of development had been destroyed. That finding eventually led to the passage of the Bayh-Dole Act, which restored the incentives of our patent system needed for effective public/private sector partnerships. Those alliances make the United States the unquestioned leader in the life sciences.

While partnerships between our academic research institutions, federal laboratories, and the private sector are critical, industry is assuming the risk. Those risks are particularly heavy on the small companies which drive innovation, especially when it comes to developing new drugs. The U.S. is the only country in the world where small companies routinely play crucial roles in creating breakthrough drugs.

Despite the tremendous successes of our system, those who want to return us to the pre-Bayh-Dole era claim that the government is "derisking" inventions it helps to create, giving developers an unfair advantage. That is demonstrably false.

Government discoveries are embryonic, more like ideas than products. That is particularly true for developing new drugs. A new [study](#) "The Relative Contributions of NIH and Private Sector Funding to the Approvals of New Biopharmaceuticals" examined the investment of NIH and industry in 18 FDA-approved

therapies, which cited NIH-supported inventions. NIH provided \$0.670 billion in funding against \$44.3 billion from private industry. And even that can be misleading, as the vast majority of new therapies fail in the development pipeline. Industry eats those costs.

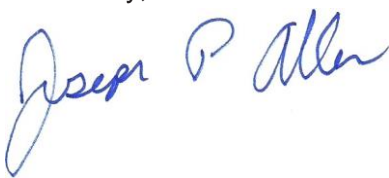
The other fallacy is that companies are lined up to partner with NIH or academic research centers. As those running your programs will attest, most times, it is very difficult to find even one company willing to assume the burden of taking a government-funded invention to market. That's particularly true for drug development because of the enormous costs, decades of research required, and uncertainties in obtaining FDA approval. No company gets an "express lane" because they are working on a government-supported invention.

One of America's key advantages over our foreign competitors is that our system provides the authorities and incentives for entrepreneurial companies to develop government-funded inventions. That makes federal programs more effective at no cost to taxpayers. Companies assume this burden knowing the odds are stacked against them. If we want to continue to be the innovation wonder of the world and the source of new drugs and other therapies, the last thing we should do is make those burdens even heavier.

For these reasons, I urge you not to use the fact that a company beat the odds and made it across the finish line against them in negotiating Medicare drug prices. Any benefits in short-term price reduction will be massively offset by those walking away from working with NIH and our research universities in the future.

That's a price we simply cannot afford to pay.

Sincerely,



Joseph P. Allen
Executive Director
Bayh-Dole Coalition

Tuesday, April 11, 2023

SENT VIA ELECTRONIC DELIVERY:

IRARebateandNegotiation@cms.hhs.gov

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue SW
Washington, DC 20201

Subject: Medicare Drug Price Negotiation Program Guidance

Dear Honorable Brooks-LaSure:

Bellus Health Inc. appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance). At Bellus Health, we are working to better the lives of patients suffering from persistent cough, starting with the development of camlipixant (BLU-5937) for the treatment of refractory chronic cough. As a relatively small biotech, we are solely focused on developing pharmacologic innovations that address unmet needs for patients. Although we acknowledge the previously stated CMS position that guidance in the CMS Medicare Drug Price Negotiation Program is final, we consider key provisions within Section 30 and other sections to be concerning and hinder our ability as a company and industry to continue to provide patients in need of solutions with medical innovations.

In particular, we would like to draw attention to the following provisions:

- I. Section 30.1 Medicare negotiation for NDA-path drugs at nine-years post launch
 - a. Bellus Health, Inc. is currently developing camlipixant (BLU-5937) for the treatment of refractory chronic cough, to which there is currently no indicated treatment available for patients. Reducing our ability to recover investment before eligibility to NDA-path negotiations in 9-years inhibits our ability to fuel further discovery and development. This directly disincentivizes investment in and steers funding away from such small molecule innovations like camlipixant (BLU-5937) and across the industry, even though the development costs and risks have not changed. We ask that you strongly consider changing the timing for NDA-path negotiations from 9-years to the same 13-year period as that for BLA-path drugs. While this is still less than the typical 14-years of marketing exclusivity afforded by patent protection, this adjustment is more logical, allowing investment to recalibrate slightly to one less year as opposed to 5 years.

.../2



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- II. Section 50.2 CMS' process for determining the Maximum Fair Price for individual medicines as well as the relevance of "therapeutic alternatives" to the drugs it selects for negotiation
- a. As a company focused on the patient, we are concerned that patient-centric outcomes are not adequately weighted in traditional cost-effectiveness analyses. Cost-effectiveness approaches embraced by ICER in the US and formal HTA bodies outside of the US exclude many demonstrable benefits of medical innovations, resulting in considerable underestimation of the true value of medicines. To the extent that CMS intends to consider the value that medical innovations bring to society before determining how aggressively to lower the price, CMS should include more comprehensive value elements, such as using a dynamic stacked cohort model that includes value to patients, caregivers, and the population whose risk are reduced by including the innovation. Choosing not to do so would result in applying over-simplified math that inherently undervalues innovations, signaling to investors that the value of new innovations will be underestimated and not reward development costs and risks.

We appreciate your consideration of our comments as you develop the Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact the undersigned by telephone at +1 (450) 680-4551 or by e-mail at rbelini@bellushealth.com if you have any questions regarding our comments.

Sincerely,

/s/-

President and CEO



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April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Submitted electronically

Dear Administrator:

Biocom California appreciates the opportunity to offer comments on the initial guidance issued by the Centers for Medicare and Medicaid Services (CMS) for the implementation of the Medicare Drug Price Negotiation Program (“Negotiation Program”)¹.

Biocom California is the largest, most experienced leader and advocate for California’s life science sector, which includes biotechnology, pharmaceutical, medical device, genomics and diagnostics companies of all sizes, as well as research universities and institutes, clinical research organizations, investors and service providers. With more than 1,700 members dedicated to improving health and quality of life, Biocom California drives public policy initiatives to positively influence the state’s life science community in the research, development, and delivery of innovative products. California’s life sciences industry generates over \$375 billion in annual economic activity, supports 435,000 jobs, and increases labor income by \$115 billion per year².

While Biocom California supports the Inflation Reduction Act’s (IRA) establishment of a \$2,000 cap on out-of-pocket patient spending and the restructuring of the Medicare Part D benefit program, we have continuously raised strong concerns about the Medicare Negotiation provisions which will have a devastating impact on current and future biotechnology innovation. We believe that the IRA does not balance promoting patient affordability and the role of the biomedical community in bringing innovative medicines to market. As the advocate for California’s life science sector, we understand the importance for stakeholders to inform and guide the establishment of the Negotiation Program and we offer our comments below:

¹ Federal Register, 87 FR 30963, pp. 30963-30966, May 20, 2022.

² Biocom California 2022 Economic Impact Report Databook. <https://www.biocom.org/eir/>

Biocom California is disappointed by the agency’s decision not to accept comments on Section 30, *Identification of Selected Drugs for Initial Price Applicability Year 2026*. We believe stakeholders should have the opportunity to provide feedback on all aspects of this program. This initial approach to developing the framework sets an unfavorable precedent of limited communication and a lack of transparency between CMS and stakeholders. **We encourage the agency to consider comments on all sections of this initial guidance in order to prioritize transparency and engagement with stakeholders. We respectfully submit the following comments on Section 30 and request consideration:**

Identification of Qualifying Single Source Part D Drugs for Initial Price Applicability Year 2026

The guidance states that CMS will identify a potential qualifying single source drug by “all dosage forms and strengths of the drug with the same active moiety and the same holder of a New Drug Application (NDA), inclusive of products that are marketed pursuant to different NDAs.” For biological products, CMS will consider “all dosage forms and strengths of the biological product with the same active ingredient and the same holder of a Biologics License Application (BLA) inclusive of products that are marketed pursuant to different BLAs.”

Biocom California disagrees with CMS’s approach to identifying a qualifying single source drug and its dosage forms and strengths by its common active moiety and common active ingredient for drugs and biologics, respectively. Instead, we suggest that CMS identify drugs and their dosage forms and strengths by referencing an NDA or BLA. The Food and Drug Administration’s (FDA) application-based framework should act as a reference and be adopted such that a product approved or licensed under a new NDA or BLA (as opposed to a product approved or licensed under a supplement to an existing NDA or BLA) is a distinct qualifying single source drug. Utilizing this framework to distinguish products would be consistent with industry practice and incentivize innovation; unlike CMS’s current definition of a “qualifying single source drug” which combines drug products by common active moiety and biological products by common active ingredient. Furthermore, utilizing FDA’s application-based framework would enable CMS to more easily identify relevant dosage forms and strengths when aggregating Medicare expenditures and this would allow manufacturers to track the seven- or eleven-year “qualifying single source drug” clock more readily.

Orphan Drug Exclusion from Qualifying Single Source Drugs

In section 30.1.1, CMS explains that certain orphan drugs will be excluded when identifying qualifying single source drugs: “CMS will exclude a drug or biological product that is designated as a drug for only one rare disease or condition under section 526 of the [Food, Drug, and Cosmetics] FD&C Act and that is approved for only an indication (or indications) for such disease or condition.” The limited scope of the orphan drug exclusion risks disincentivizing orphan drug research and development (R&D) and will impact a manufacturer’s decision to continue follow-on R&D to expand a drug’s indications to include additional rare diseases. The initial guidance also states, “CMS is considering whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development.” **Biocom California urges CMS to consider ways to expand the orphan drug exclusion to allow orphan drugs and biological products with multiple rare disease indications to qualify for the exclusion.** By expanding the scope of orphan drug exclusion, CMS would continue to support and incentivize the development of orphan drugs and rare disease R&D.

Additionally, in situations where an approved indication falls within the scope of an orphan drug designation but there is no corresponding orphan exclusivity, CMS cannot rely on FDA's databases as they track orphan exclusivity, rather than a designation, to determine eligibility for orphan drug exclusion. **Biocom California suggests that CMS establish a process that enables manufacturers to submit evidence demonstrating that an indication falls within an orphan drug designation in situations where the agency is unable to determine eligibility for the exclusion based on FDA's databases.** We encourage CMS to establish this process in a timely manner so that manufacturers can gather evidence supporting eligibility for the orphan drug exclusion in advance of the first selected drug publication date.

Furthermore, under FDA regulations, a manufacturer may voluntarily withdraw a requested or granted orphan drug designation at any time and the withdrawal is publicized. **We ask CMS to clarify that, when determining eligibility for the orphan drug exclusion, the eligibility will be based on orphan drug designation *at the time of selection* and will not reference any prior designation that has been withdrawn.** This practice would continue to protect the scope of orphan drugs eligible for the exclusion.

Lastly, Biocom California asks CMS to clarify that, where an orphan drug loses eligibility for the orphan drug exclusion, the seven- or eleven-year "qualified single source drug" clock runs from *the date on which the drug lost eligibility for the exclusion*. An orphan drug that loses eligibility for the orphan drug exclusion due to an expansion of indications for a second rare disease could be immediately eligible for negotiations. **This would further disincentivize drug developers from investing in rare disease R&D and we ask CMS to clarify these details in order to mitigate the risk that the Negotiation Program will deter necessary orphan drug development.**

Exception for Small Biotech Drugs

Per the IRA, a drug is exempt from negotiation for initial price applicability years 2026, 2027, and 2028 if the drug meets the exception for small biotech drugs ("Small Biotech Exception"). For initial price applicability year 2026, wherein only Part D drugs will be selected for negotiation, this exception requires that in 2021, "the Total Expenditures under Part D for the qualifying single source drug (1) were equal to or less than one percent of the Total Expenditures under Part D for all covered Part D drugs; and (2) were equal to at least 80 percent of the Total Expenditures under Part D for all covered Part D drugs for which the manufacturer of the drug had a [Coverage Gap Discount Program] CGDP agreement in effect during 2021."

The Small Biotech Exception is a critical protection that recognizes the need for small biotech drugs to be exempt from negotiation. Therefore, Biocom California asks CMS to make the Small Biotech Exception permanent and to release transparent and predictable guidance that assists small biotech companies in applying for the exception. CMS has indicated that the current Small Biotech Exception information collection request (ICR) is focused only on initial price applicability in the year 2026 and the agency has not publicly announced which 2021 total expenditure data it will utilize to determine eligibility for the exception. **Without this information, it is challenging for small biotech manufacturers to determine whether a submission will be needed in the current or future years, and we suggest that CMS clearly state the specific criteria manufacturers should reference when determining whether to apply for the Small Biotech Exception. For initial price applicability year 2026, we recommend that manufacturers who believe they qualify for the Small Biotech Exception should apply and be approved for this exception this year regardless of whether the drug meets the test of a high spend drug under Sec. 1192 (d)(1)³.** This will benefit small biotech manufacturers who have a limited number of products on the market.

³ Social Security Act § 1192(d)(1)

Section 30.2.1 of the guidance states: “To receive consideration for the Small Biotech Exception for initial price applicability year 2026, the Submitting Manufacturer must submit the Small Biotech Exception Information Collection Request Form using the CMS Health Plan Management System (HPMS) by the deadline established by CMS; CMS anticipates that this deadline will be in June 2023 but will publish a specific deadline on the CMS IRA website in the future. This due date will be in advance of the date on which CMS is required to publish the list of selected drugs for initial price applicability year 2026 and will allow sufficient time for CMS to consider whether the qualifying single source drug qualifies for the Small Biotech Exception.”

Biocom California appreciates the agency’s transparency in providing an anticipated date for the deadline to submit for the Small Biotech Exception. **We ask that CMS publish the specific June 2023 deadline date on the IRA website as soon as possible so manufacturers can have adequate notice of the ICR form submission date and can plan their efforts accordingly. Additionally, we ask CMS to clearly specify the review and response timelines (in situations where the agency does and does not grant the exception) for submitting manufacturers as far in advance of September 1, 2023, as possible.** If a negative determination is granted, CMS’s response should include 1) a rationale in sufficient detail explaining how the determination was made and 2) information regarding which expenditure data was referenced that led to a negative determination.

We also encourage the agency to develop a dispute resolution process that enables manufacturers to respond to and appeal a negative determination. As part of this process, CMS should engage in a dialogue and small biotech companies should have the opportunity to provide additional data to support their application for the exception before CMS provides a final determination. **If a manufacturer has previously received the Small Biotech Exception and there has been no significant change in the manufacturer’s circumstances, Biocom California asks that manufacturers need not reapply for the Small Biotech Exception in subsequent years and, instead, inform CMS annually that no changes have occurred.**

Lastly, Biocom California would like to underscore the importance of maintaining the confidentiality of proprietary information; especially when submitted as part of the Small Biotech Exception ICR. **We ask that CMS provide more specific information regarding its approach for publicly sharing which small biotech drugs qualify for the exception. In order to promote transparency and consistency, we recommend the agency publish a summary list of the small biotech drugs and manufacturers that qualify each year.** Any additional information detailing how or why a specific manufacturer’s drug qualified should only be released with the manufacturer’s consent as this will ensure proprietary information remains protected.

Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026

In section 40.1, CMS states that it “will make reasonable efforts to make the final text of the Agreement available to the public before the selected drug list for initial price applicability year 2026 is published.” **Biocom California requests that CMS publicly release and provide an opportunity to comment on the text of the Negotiation Program Agreement as soon as possible, and well in advance of September 1, 2023, when CMS publishes the selected drug list.** It is imperative that manufacturers have an adequate opportunity to review the agreement and understand their specific obligations since they are subject to civil monetary penalties (CMPs) if in violation of the agreement’s terms. Furthermore, advanced notice of the agreement is necessary for manufacturers to establish new processes in order to comply with the terms of the agreement.

Confidentiality of Proprietary Information

In section 40.2.1, CMS explains that it “intends to implement a confidentiality policy that is consistent with existing requirements for protecting proprietary information, such as Exemption 4 of [the Freedom of Information Act] FOIA.” The guidance states that R&D costs and recoupment, unit costs of production and distribution, pending patent applications, market data, revenue and sales volume data will be considered proprietary. Conversely, data on prior Federal funding, approved patent applications, exclusivities, and FDA applications and approvals will be considered non-proprietary since this data is publicly available. **Biocom California acknowledges and agrees with the information that will be considered proprietary versus non-proprietary. However, we believe there is a need for CMS to further explain how it intends to protect a manufacturer’s confidential information and establish more robust safeguards to ensure that the agency is adequately handling proprietary information submitted as part of the negotiation process. We suggest that CMS focus on developing data privacy and security protection protocols that include robust storage and controls that limit access to confidential information to CMS staff on a “need-to-know” basis.**

Furthermore, the initial guidance outlines that “CMS is required to publish the explanation for the MFP [maximum fair price] by March 1, 2025, for initial price applicability year 2026 (see section 60.6.1 of this memorandum). In this public explanation and any other public documents discussing the MFP, CMS intends to make high-level comments about the data submitted to CMS, without sharing any proprietary information reported to CMS under section 1193(a)(4) for purposes of the negotiation.” **Biocom California appreciates CMS’s discretion and intention to only make high-level comments regarding the submitted data. However, the possibility of inadvertently disclosing confidential information is possible. In order to avoid such a disclosure, we suggest CMS allow manufacturers the opportunity to review a draft explanation of the MFP prior to its publication and dispute any confidentiality concerns. This will ensure that manufacturers are comfortable with the information disclosed and no proprietary information is inadvertently released.**

In section 40.2.2, the Primary Manufacturer is barred from disclosing “any information in the initial offer or any subsequent offer by CMS, the ceiling price contained in any offer, or any information contained in any concise justification provided with an offer,” as well as “any information exchanged verbally during the negotiation period.” CMS also proposes to require that manufacturers destroy information if the drug or biologic no longer qualifies as a selected drug. However, Congress, through the IRA, did not authorize CMS to impose these mandatory non-disclosure and information-destruction provisions. These provisions violate manufacturers’ rights to free speech and are not necessary to administer or monitor compliance with the Negotiation Program. Moreover, this practice would put manufacturers at an unnecessary disadvantage that hinders the program’s administration, efficiency, and consistency. **In order to facilitate a fair and transparent negotiation process, we ask CMS to remove the non-disclosure and information-destruction provisions.**

Providing Access to the MFP

In section 40.4, CMS details the ways in which a Primary Manufacturer may provide access to the MFP by either “(1) ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP; or (2) providing retrospective reimbursement for the difference between the dispensing entity’s acquisition cost and the MFP” within 14 days. **Biocom California supports CMS’s proposed MFP rebate approach and appreciates the agency’s flexibility for manufacturers. In order to facilitate access to the MFP, we ask that CMS make available the necessary datasets for manufacturers to ensure that the MFP discount is being provided on an MFP-eligible product to an MFP-eligible patient.**

Additionally, the initial guidance does not specify when the 14-day retrospective reimbursement timeframe begins, and **we ask CMS to confirm that the proposed 14-day period begins on the date on which the manufacturer has validated the eligibility of an MFP-eligible individual. We also urge the agency to lengthen this timeframe and seek additional stakeholder input to determine a more appropriate timeline. Given the new processes that still need to be developed as part of the Negotiation Program, we ask CMS for maximum flexibility to ensure program compliance.**

Manufacturer Specific Data

Section 50.1 of the initial guidance outlines the selected drug data requirements to be reported by the Primary Manufacturer to CMS by October 2, 2023. These elements include 1) “research and development costs of the Primary Manufacturer...and the extent to which the Primary Manufacturer has recouped those costs;” 2) “current unit costs of production and distribution...averaged across the Primary Manufacturer and any Secondary Manufacturer(s);” 3) “prior Federal financial support for novel therapeutic discovery and development with respect to the selected drug;” 4) “data on pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the FD&C Act or section 351(a) of the PHS Act;” and 5) “market data and revenue and sales volume data for the selected drug in the United States for the Primary Manufacturer and any Secondary Manufacturer(s) (with the exception of costs related to the acquisition of the selected drug, which would be reported only for the Primary Manufacturer).”

While we appreciate CMS outlining the exact manufacturer-specific data required, it is unclear what the agency’s expectations are regarding data quality and how it intends to assess these factors without standardizing each element. For example, R&D costs related to the selected drug may have been incurred via disease-specific research programs that evaluated multiple drugs with varying indications. It would be difficult for a manufacturer to calculate the exact R&D costs for a selected drug that was part of a larger disease research program. **In an effort to provide clear data that aligns with the relevant information CMS requires, we suggest that the agency allow manufacturers to 1) submit the information which they believe is most relevant and aligns with these required elements and 2) provide a justification for the manufacturer-specific data they submitted.**

Moreover, we urge CMS to reconsider its proposal that if the selected drug has patents and exclusivities that will last for several years, CMS may consider adjusting the preliminary price downward. This proposal, which the agency did not provide a rationale for, will likely discourage innovation by penalizing innovators from obtaining patents. Additionally, the proposal fails to consider a key value of the patent right as a patent is a quid pro quo situation. In exchange for the right to exclude for a limited period of time, the inventor must fully disclose their invention such that the public can benefit from it and expand on it. Therefore, a patented product creates an economic value derived from its improved technological features and social value through its public disclosure. **We recommend CMS consider the value associated with a patented product and urge the agency not to use patent coverage as a downward adjustment factor.** Further, the CMS proposal may be inconsistent with the United States’ obligation under the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement⁴. Specifically, Article 30 of the TRIPS agreement requires that each member state “not unreasonably conflict with a normal exploitation of the patent and ... not unreasonably prejudice the legitimate interests of the patent owner.” Adjusting a price downward in view of patent coverage appears to be inconsistent with this TRIPS requirement.

⁴ Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 1869 U.N.T.S. 299, 33 I.L.M. 1197 (1994)

Lastly, Biocom California also asks CMS to clarify how it intends to consider pending patent applications as a negotiation factor when determining a preliminary price. We discourage the agency from utilizing pending applications as a factor to downward-adjust prices since these may not always mature into a full patent and do not guarantee protection for the product.

Evidence about Clinical Benefit for the Selected Drug

As noted in section 50.2, CMS will “consider evidence about alternative treatments to the selected drug, as available, including:

1. The extent to which the selected drug represents a therapeutic advance compared to existing therapeutic alternatives for the selected drug and the costs of such existing therapeutic alternatives;
2. FDA-approved prescribing information for the selected drug and its therapeutic alternatives;
3. Comparative effectiveness of the selected drug and its therapeutic alternatives, including the effects of the selected drug and its therapeutic alternatives on specific populations (including individuals with disabilities, the elderly, the terminally ill, children, and other patient populations, herein referred to as “specific populations”); and
4. The extent to which the selected drug and the therapeutic alternatives to the drug address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy.”

Additionally, CMS will not use “evidence from comparative clinical effectiveness research in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill” and certain uses of quality-adjusted life-years (QALYs) will not be used in the negotiation process. Furthermore, in section 60.3 *Methodology for Developing an Initial Offer*, when developing a starting point for the initial offer, CMS proposes to utilize the net price for identified therapeutic alternatives and, after the review of the clinical evidence, adjust this price to develop a “preliminary price.” At this point, CMS will then consider the manufacturer-specific data to adjust the preliminary price upward or downward. When there is no therapeutic alternative CMS would adjust the starting point based on how the selected drug fills an unmet medical need.

Biocom California supports CMS’s proposed approach of prioritizing a selected drug’s therapeutic benefit and negotiation factors related to therapeutic alternatives, comparative effectiveness, and unmet need. Ensuring such evidence is appropriately weighted in the MFP will more appropriately reward products that have enhanced patient care and will help maintain the investment in promising R&D and clinical programs. **Since CMS proposes to adjust the starting point for the initial offer based on its review of clinical benefit evidence, Biocom California encourages an approach that places a greater emphasis on a range of high-quality robust evidence, including real-world evidence (RWE), and prioritizes information submitted by manufacturers with expertise in their therapeutic areas.** We suggest the agency provide additional clarifying information about how it will evaluate alternative treatment evidence from different stakeholders and how that data will be considered when determining the MFP. Lastly, in order to promote a transparent negotiation process, we ask CMS to provide manufacturers with details regarding the agency’s evaluation of evidence related to therapeutic alternatives and discuss this analysis with manufacturers before CMS’s initial offer in February 2024.

Negotiation Process

In section 60, CMS outlines the methodology and negotiation process that it intends to use to “achieve the lowest maximum fair price for each selected drug.” After the written initial offer from CMS is presented to the Primary Manufacturer, the negotiation process would begin as described in section 60.4 of the initial guidance. As part of this process, the Primary Manufacturer may provide an optional written counteroffer (if CMS’ written initial offer is not accepted) that must be submitted no later than 30 days after the date of receipt of the written initial offer. CMS may then provide a written response to the optional written counteroffer and, if the Primary Manufacturer’s counteroffer is not accepted by the agency, up to three possible in-person or virtual negotiation meetings may take place. At the conclusion of these meetings between the Primary Manufacturer and CMS, the agency will provide a final written offer to the manufacturer, and they must either accept or reject this final offer before the end of the negotiation period.

Biocom California encourages an open and transparent dialogue between CMS and the Primary Manufacturer when determining the MFP. As part of the Negotiation Process, we believe CMS should begin at the MFP ceiling price instead of negotiating upwards from the lowest MFP. We also suggest the agency consider circumstances when drugs should be priced as close as possible to the MFP ceiling in order to avoid imperiling patient access. Additionally, to facilitate a transparent negotiation process, we ask CMS to provide 1) a meaningful justification of its initial offer, 2) its response to any counteroffer, and 3) afford the manufacturer a legitimate opportunity to comment on the response before the MFP is set. As part of this justification, we would ask the agency to provide a rationale as to how it arrived at the offer or response, including an explanation of how the decision is supported by the negotiation factors, how those factors were considered and weighted, and any additional information that was utilized as a part of the decision. Disclosing the basis of an offer or response would promote a robust and effective dialogue that informs more targeted discussions during the negotiation process.

Lastly, the initial guidance specifies that, only in the case where CMS rejects a counteroffer, the agency will extend an invitation for a negotiation meeting within 30 days of receipt of the counteroffer. **Biocom California asks that the agency fulfill its commitment to responding to counteroffers within 30 days and allow the Primary Manufacturer at least 30 days to comment on CMS’s response before the MFP is set.** These actions would further support a consistent and transparent negotiation process and prevent the MFP from being finalized based on an error or lack of information.

Removal from the Selected Drug List Before or During Negotiation, or After an MFP is in Effect

In section 70, CMS explains that a drug will be removed from the selected drug list and no longer subject to the negotiation process when the agency determines that “(1) the FDA has approved a generic drug under section 505(j) of the FD&C Act that identifies as its reference listed drug a product that is included in the selected drug, or the FDA has licensed a biosimilar biological product under section 351(k) of the PHS Act that identifies as its reference product a product that is included in the selected drug; and, (2) the generic drug or biosimilar biological product, as applicable, is marketed pursuant to such approval or licensure.” CMS intends to review prescription drug event (PDE) data to determine whether a generic drug or biosimilar biological product is approved and marketed. The agency will consider a generic or biosimilar to be marketed when PDE data reveals that the manufacturer has engaged in bona fide marketing of that drug or product.

Biocom California disagrees with the agency’s use of “bona fide marketing” as this is a subjective assessment of “robust and meaningful competition” and the initial guidance lacks objective, clear criteria defining this standard. We suggest CMS abandon “bona fide marketing” and, instead, consider a product’s market date as the date on which a generic or biosimilar is marketed and the date on which CMS *determines* that a generic or biosimilar has been marketed.

Per CMS’s Medicaid Drug Rebate Program (MDRP) Data, “market date” is defined as “the earliest date the drug was first marketed under the application number by any labeler⁵.” The MDRP “market date” is a familiar term for both CMS and manufacturers and would allow for a consistent application and less burdensome adoption of this standard as part of the Negotiation Program.

Furthermore, the use of PDE data raises timing concerns as there will be a delay between the actual date of marketing and the date of CMS’s determination that a product has been marketed since some time is required for sales to be reflected in this data. Furthermore, when a new product is available and actively marketed, it takes time for the widespread adoption of the product by providers and for patients to transition to the generic or biosimilar. During this uptake period, this information will not be immediately reflected in the PDE data once a generic or biosimilar is on the market.

Manufacturer Compliance and Oversight

In section 90.2, *Monitoring of Access to the MFP*, the initial guidance explains that “CMS intends to require that the Primary Manufacturer establish safeguards to ensure the MFP is available to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers on units of the selected drug for which there are Secondary Manufacturers, as described in section 40.4 of this memorandum.” Additionally, CMS explains that “each component of the pharmaceutical supply chain may have a role in making the MFP available to MFP-eligible individuals, but it is ultimately the Primary Manufacturer’s responsibility to ensure access to the MFP.”

Biocom California is concerned with the large responsibility placed on the Primary Manufacturer to ensure that entities across the entire supply chain have made the MFP available to MFP-eligible individuals. When there are multiple Secondary Manufacturers involved such as repackers and relabelers, it is unrealistic to hold the Primary Manufacturer solely responsible for the compliance of these entities. Furthermore, Primary Manufacturers do not have visibility into a Secondary Manufacturer’s information, thus making this policy nearly impossible to comply with. The initial guidance explains that a manufacturer who does not comply with certain Negotiation Program deadlines and requirements could be subject to excise tax liability or CMPs. **We do not believe that Primary Manufacturers should be penalized due to a lack of data access and business practices that they cannot enforce. We strongly suggest that CMS not hold a Primary Manufacturer responsible for ensuring the compliance of Secondary Manufacturers and, instead, Secondary Manufacturers should be held responsible and subject to CMPs themselves if they do not provide access to the MFP. Lastly, we ask CMS to require other stakeholders (i.e., providers, health plans, etc.) to make data available so that manufacturers can comply with the MFP effectuation.**

⁵ CMS, MDRP Data Guide § 5.15 (Apr. 2022).

Biocom California comments on the Medicare Drug Price Negotiation Program

We appreciate the opportunity to provide feedback on behalf of our members and thank you for your time and diligence in examining our comments. Please contact Biocom California's Associate Manager of Regulatory Policy, Zoe Bilis, at zbilis@biocom.org for additional information or questions. We look forward to continuing to work with you on this matter.

Sincerely,

A handwritten signature in black ink, appearing to read "Joe D. Panetta". The signature is fluid and cursive, with the first name "Joe" and last name "Panetta" being more prominent.

Joe Panetta
President and CEO
Biocom California



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April 14, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244–1850

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

The Biotechnology Innovation Organization (BIO) appreciates this opportunity to comment on the initial guidance regarding the Drug Price Negotiation Program (Negotiation Program) under the Inflation Reduction Act of 2022 (IRA) issued by the Centers for Medicare & Medicaid Services (CMS or Agency) on March 15, 2023 (Initial Guidance).¹

BIO is the world’s largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than thirty other nations. BIO’s members develop medical products and technologies to treat patients afflicted with serious diseases, delay the onset of such diseases, or prevent them in the first place. As a result, our members’ novel therapeutics, vaccines, and diagnostics not only have improved health outcomes but also have reduced health care expenditures due to fewer physician office visits, hospitalizations, and surgical interventions. BIO’s members include biologic and vaccine manufacturers, which have worked closely with stakeholders across the spectrum, including the public health and patient advocacy communities, to support policies that help ensure access to innovative and life-saving medicines and vaccines for all individuals.

BIO appreciates the steps the agency has taken to establish a dialogue with key stakeholders about the Negotiation Program and other elements of the IRA, but we have significant concerns about the Initial Guidance and the limitations on comments CMS has imposed.

We also believe it’s imperative to underscore our views on the IRA. We have long supported a Medicare Part D out-of-pocket cap and the ability for patients to spread these costs throughout the year. These

¹ CMS, Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (Mar. 15, 2023), *available at* <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.



are essential patient protections. At the same time, we believe that patient out-of-pocket costs will never be truly addressed unless the broken rebate system – which benefits pharmacy benefit managers (PBMs) over patients – is addressed. PBMs continue to leverage their size and market influence to ensure they can rake in enormous profits, and they do so at the expense of vulnerable patients.

In addition, we are very concerned about the significant and negative impacts the IRA will have on companies' investments in research and development, which in turn will harm beneficiary access to future treatments and cures, particularly for rare, hard-to-treat diseases and those areas with high unmet need. We continue to urge CMS to consider these impacts as the agency works to update this proposed guidance based on stakeholder feedback.

We also note our strong disappointment that key aspects of this guidance have been issued as final without soliciting comment, which is a concerning step backward from CMS's stated commitment to transparency. BIO strongly urges the Agency to consider stakeholder comments on all aspects of the Initial Guidance. Notably, despite previously committing to "prioritiz[ing] transparency and robust engagement" in its implementation of the Negotiation Program,² the Agency solicits comment on only certain policies, and finalizes other policies with no opportunity for comment—specifically, the foundational policies set forth in Section 30 of the Initial Guidance.³ The Agency's own stated goals of transparency and engagement require immediate reconsideration of this ill-advised start to the Agency's stewardship of the Negotiation Program.

BIO and our members have long argued that the underlying structure of the negotiation program, as set forth by the statute and implemented here by CMS, is legally flawed. In review of the punishing penalties for non-compliance, and the general inflexibility of the process for product selection and maximum fair price (MFP) implementation, these legal flaws cannot be overcome through general guidance clarity at this stage. Nevertheless, we provide herein several suggestions for CMS to consider that might be helpful in the transparency objective of the Agency as it implements this program. None of these resolve the more fundamental legal infirmities of the overall program, nor could they.

We outline below how the implementation of the Negotiation Program would materially benefit from two-sided engagement on all topics, including both a full opportunity for stakeholders to submit comments on proposed policies and meaningful responses to such comments that demonstrate the Agency's consideration of the points made and reveal the reasoning underlying the Agency's final

² CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026 (Jan. 11, 2023), available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf>.

³ While BIO understands that the policies set forth in Section 30 of the Initial Guidance are final and that CMS is not soliciting comment on such policies, BIO sets forth herein for the record the comments that it would have made had CMS solicited comment.



decision-making. Such an approach would fulfill the purpose of a comment period: to enable “[t]he interchange of ideas between the government and its citizenry[, which] provides a broader base for intelligent decision-making and promotes greater responsiveness to the needs of the people.”⁴ The need for such a fulsome process is especially acute here, given the novelty and complexity of the Negotiation Program; the vast ramifications that the program will have for patients, providers, pharmacies, manufacturers, and countless other stakeholders; and the potentially profound negative repercussions for patient access to needed therapies that could follow from errors, misunderstandings, or gaps in understanding. In these circumstances, the Agency should maximize transparency and engagement in its decision-making process, including by both affording a full opportunity for comment and meaningfully responding to stakeholder feedback.

This includes ensuring the negotiation process is transparent, predictable, and fair, with CMS providing necessary accountability to stakeholders and clarifying how it will consider and utilize the broad set of information it will collect and review related to the negotiation factors. Further, we continue to urge CMS to emphasize factors that are critical for patients, specifically factors related to clinical benefit and unmet medical need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.

We also urge CMS to eliminate its proposed, one-sided requirement that manufacturers destroy all records related to the negotiation process and submit a Certificate of Data Destruction to CMS certifying that all information received from CMS during the negotiation period and potential renegotiation period(s) was destroyed. Basic due process mandates that manufacturers be given the ability to maintain records related to negotiation proceedings. Moreover, BIO opposes the blanket prohibition on manufacturers from disclosing or otherwise publicizing information “in the initial offer, including the ceiling price, or the concise justification from the Secretary or any subsequent offer of concise justification, nor information derived from those justifications or offers...”. This one-sided information control heightens the ultimate public complaint that the entirety of the “negotiation” process is anything but actual “negotiation.” BIO disagrees with this approach and recommends CMS abandon it.

We also recommend that CMS finalize the Initial Guidance well in advance of the selected drug publication date for initial price applicability year (IPAY) 2026 to ensure that all stakeholders have ample time before such date to fully digest the contents of the finalized guidance and conform their actions accordingly. Similarly, CMS should solicit comment on proposed guidance applicable to IPAY 2027 and IPAY 2028 (the first IPAY applicable to Medicare Part B drugs) as soon as reasonably possible and well in advance of the selected drug publication dates for such IPAYs.

⁴ *Buschmann v. Schweiker*, 676 F.2d 352, 357 (9th Cir. 1982) (internal quotation marks and citations omitted).



Below please find an overview of our recommendations; our more detailed comments follow.

Regarding the definitions of qualifying single source drugs and negotiation eligible drugs:

- BIO strenuously disagrees with CMS's approach to identifying a qualifying single source drug by reference to common active moiety (drugs) or common active ingredient (biologics). Both law and policy dictate that a qualifying single source drug be identified by reference to its NDA or BLA.
- CMS should clarify the scope of the orphan drug exclusion in a manner that maximizes protections for orphan drugs.
- CMS should take steps to make the process to qualify for the small biotech exception more transparent and predictable.

Regarding the selection, and delayed selection, for negotiation, CMS should:

- Provide for a pre-selection process where, well in advance of the selected drug publication date, CMS would notify each manufacturer of each drug that it intends to select for negotiation and afford each manufacturer a dispute process.
- Improve the process by which a biosimilar manufacturer may request a delay in the selection of a reference product for negotiation due to anticipated biosimilar market entry. This includes providing a meaningful opportunity to request a delay, allowing for a dispute resolution process, and considering all information submitted by a biosimilar manufacturer.

In implementing the negotiation process, CMS should:

- Provide for robust and meaningful engagement and dialogue between the Agency and the manufacturer throughout the negotiation process.
- Allow manufacturers to supplement timely submissions where a post-submission development arises or there otherwise is good cause.
- Provide a meaningful justification of its initial offer and its response to any counteroffer and afford the manufacturer a meaningful opportunity to comment on the response the MFP is set.
- Provide more fulsome safeguards to ensure that the Agency is adequately protecting the confidentiality of all proprietary information submitted to CMS as part of the negotiation process.
- Withdraw its overly broad confidentiality obligations imposed on manufacturers.

In setting the MFP, CMS should:

- Impose on itself bright-line limitations that mitigate the negative effect of the MFP on patient access and on therapeutic innovation.
- Commit to setting the MFP at a price that will not imperil patient access.



- Ensure that the MFP is not set below the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.
- Ensure that the MFP is not set below the MFP ceiling during any year of the price applicability period into which patent protection extends.
- Ensure that the MFP is set at the MFP ceiling until at least the first year during the price applicability period that starts after the date on which the most recently approved indication is thirteen years post-approval.
- Ensure the MFP is not set below the MFP ceiling for vaccines recommended by the Advisory Committee on Immunization Practices (ACIP) at the Centers for Disease Control (CDC).
- Ensure predictable, transparent engagement with manufacturers regarding how the MFP was set.

In utilizing the negotiation factors, CMS should:

- Ensure a transparent, fair, and predictable process.
- Emphasize factors related to clinical benefit and unmet need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.
- Utilize a more robust definition of unmet medical need.
- Clarify how it will evaluate the evidence about alternative treatments by different stakeholders and how different evidence will be considered in setting the MFP.
- Ensure that a robust, comprehensive set of information submitted by manufacturers– with any necessary supplemental material – will be accepted and considered by CMS.
- Allow manufacturers to use reasonable assumptions regarding the information they submit on the manufacturer-specific data.
- Reject approaches that would reduce the preliminary price when a drug has available patents and exclusivities.
- Eliminate reporting and other requirements under the Primary Manufacturer/Secondary Manufacturer Construct.

In establishing the MFP Ceiling, CMS should:

- Abandon its proposal to create a new price point calculated based on the four quarters of a calendar year, and instead simply adopt the existing annual Non-FAMP.
- Establish an exceptions process to account for restatements and anomalies.
- Confirm if the time period for determining whether a selected drug is an extended- or long-monopoly drug runs to the start of the applicable IPAY or the selected drug publication date.
- Calculate the MFP ceiling for Part D drugs exclusive of manufacturer price concessions unless they are passed through at the point of sale.



Regarding the requirement that manufacturers provide access to the MFP, CMS should:

- Finalize its proposal that access to the MFP may be provided through an MFP rebate model.
- Utilize a CMS-established third-party administrator (TPA) or clearinghouse.
- Clarify that the proposed fourteen-day period during which an MFP rebate must be paid runs from the date on which the manufacturer has validated eligibility for the rebate.
- Condition payment of a claim for reimbursement for a unit of a selected drug on the accurate use claims modifiers.
- Finalize its proposals that access to the MFP by Part D beneficiaries at the point of sale will be effectuated through plans, not manufacturers.
- Define the MFP discount using a publicly reported metric, such as wholesale acquisition cost (WAC).
- Simplify its approach for applying the MFP across dosage forms and strengths and address concerns with its proposed methodology.
- Abandon its bona fide marketing standard and instead adopt a standard that consistently designates the MDRP “market date” as both the date on which a generic or biosimilar is marketed and the date on which CMS determines that a generic or biosimilar has been marketed.

In addition, we recommend that CMS:

- Clarify that selected drugs are not subject to an inflation rebate.
- Amend its regulatory definition of “unit” to exclude MFP units from the ASP calculation.
- Proceed with caution on the implementation of CMPs and allow manufacturers a reasonable time period to cure deficiencies before CMPs are imposed.
- Ensure that the text of the Negotiation Program Agreement is made available for public comment at least sixty days in advance of the first selected drug publication date.
- Abandon its “Primary Manufacturer” and “Secondary Manufacturer” construct as part of the Agreement as it is impracticable and has no legal basis.
- Protect beneficiary access to needed therapies, including selected drugs, and implement safeguards to ensure such access.

I. Qualifying Single Source Drugs and Negotiation-Eligible Drugs

A. Background

Section 1192(e) of the Social Security Act (SSA) generally defines “qualifying single source drug” to mean:



- A drug product approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act (FDCA) and marketed pursuant to such approval where at least seven years have elapsed since the date of such approval and there is no approved and marketed generic for such product;⁵ and
- A biological product approved under section 351(a) of the Public Health Services Act (PHSA) and marketed pursuant to such licensure where at least eleven years has elapsed since the date of such licensure and there is no licensed and marketed biosimilar for such product.⁶

The statute provides for certain exclusions from the definition of “qualifying single source drug” — certain orphan drugs,⁷ plasma-derived products,⁸ and certain low Medicare spend drugs.⁹

Section 1192(d) generally defines “negotiation-eligible drug” to mean, with respect to an IPAY:

- Each of the top fifty qualifying single source drugs by Medicare Part D expenditures over a specified twelve-month period; and
- Starting with IPAY 2028, each of the top fifty qualifying single source drugs by Medicare Part B expenditures over a specified twelve-month period.¹⁰

The statute provides for the exclusion of a “small biotech drug” from the definition of “negotiation-eligible drug” for IPAYs 2026, 2027, and 2028.¹¹ Section 1192(d)(2) generally defines “small biotech drug” to mean a qualifying single source drug for which:

- The drug’s 2021 Part B or D expenditures are equal to or less than one percent of all drugs’ 2021 Part B or D expenditures; and
- The drug’s 2021 Part B or D expenditures are equal to or more than eighty percent of its manufacturer’s drugs’ 2021 Part B or D expenditures.¹²

The statute provides for the exclusion of “[a] new formulation, such an extended release formulation” from the definition of “small biotech drug.”¹³

⁵ SSA § 1192(e)(1)(A) (the seven years are counted to the selected drug publication date with respect to the applicable IPAY).

⁶ *Id.* § 1192(e)(1)(B) (the eleven years are counted to the selected drug publication date with respect to the applicable IPAY).

⁷ *Id.* § 1192(e)(3)(A).

⁸ *Id.* § 1192(e)(3)(C).

⁹ *Id.* § 1192(e)(3)(B).

¹⁰ *Id.* § 1192(d)(1).

¹¹ *Id.* § 1192(d)(2). The statute also provides for a Maximum Fair Price (MFP) floor for a “small biotech drug” for IPAYs 2029 and 2030. *Id.* § 1194(d).

¹² *Id.* § 1192(d)(2)(A).

¹³ *Id.* § 1192(d)(C).



B. Distinguishing among qualifying single source drugs and dosage forms and strengths of such drugs

It is imperative that CMS reconsider its approach to identifying a qualifying single source drug and its dosage forms and strengths by reference to common active moiety (drugs) or common active ingredient (biologics), and instead identify such a drug and its dosage forms and strengths by reference to common New Drug Application (NDA) or Biologics License Application (BLA).¹⁴

In the Initial Guidance, CMS states that it will treat products as the same qualifying single source drug where, for drug products, they share the same active moiety or, for biological products, they share the same active ingredient, and the same manufacturer holds all applicable NDAs or BLAs.¹⁵ This policy is irreconcilable with the statute.

The statute requires products to be treated as the same qualifying single source drugs only where they share the same NDA or BLA. This necessarily follows from the plain text of section 1192(e)(1). As set forth above, “qualifying single source drug” is defined for products approved under an NDA by reference to whether seven years has elapsed since “such approval;”¹⁶ likewise, the term is defined for products licensed under a BLA by reference to whether eleven years has elapsed since “such licensure.”¹⁷

Congress’s use of “such license” and “such approval” in the statute is intentional, unambiguous, and must be given effect. Congress used this language to denote that a qualifying single source drug is distinguished by a distinct approval or licensure—i.e., a distinct NDA or BLA. CMS has no authority to rewrite the plain language of the statute by inventing an ultra vires distinction between qualifying single source drugs based on their applications. Where “Congress has been unambiguous, neither the Agency nor [a] court may diverge from that intent.”¹⁸

Although the plain language of the statute is dispositive, BIO notes that other canon of statutory construction confirm Congress’s unambiguous intent to distinguish qualifying single source drugs based on distinct NDAs or BLAs and to mandate that drug and biologic products would not be subject to price controls unless a sufficient time has elapsed since “such approval” (7 years) or “such licensure” (11 years).¹⁹ Of particular note, the statute defines “qualifying single source drug” by express reference to

¹⁴ For a discussion of the related and equally critical concern with CMS’s “bona fide marketing” standard, please see section VI.F.

¹⁵ Initial Guidance at 8.

¹⁶ SSA § 1192(e)(1)(A).

¹⁷ *Id.* § 1192(e)(1)(B).

¹⁸ *Cabazon Band of Mission Indians v. Nat’l Indian Gaming Comm’n*, 827 F. Supp. 26, 29 (D.D.C. 1993), *aff’d*, 14 F.3d 633 (D.C. Cir. 1994).

¹⁹ See *Chevron v. Nat’l Res. Def. Council*, 467 US 837, 843 n.9 (1984) (in addition to the plain text, the traditional tools of statutory construction are used to ascertain the intent of Congress).



the FDCA and PHSA. It is well understood that a statute should be interpreted in the manner “most compatible with the surrounding body of law into which the provision must be integrated.”²⁰

CMS should therefore look to the well-established framework under the FDCA and PHSA for distinguishing among products. Under this framework, drug and biological products generally may be marketed only if approved or licensed by FDA,²¹ and manufacturers seeking such approvals or licensures must meet stringent requirements bearing on safety, effectiveness, and other considerations.²² In implementing this framework, FDA has spoken directly to the circumstances under which a change to an existing product is so significant that it yields a new product warranting a new NDA or BLA is, as well as the circumstances under which a change to an existing product is not.²³ It is manifestly reasonable and appropriate to rely on such FDA standards here, such that a product approved or licensed under a new NDA or BLA is a distinct qualifying single source drug.

There are immeasurable benefits to giving effect to the statute as written and, as Congress intended, adopting FDA’s application-based framework for distinguishing products (as opposed to CMS’s newly invented, statutorily unmoored scheme for doing so). First, and most critically, doing so would avoid exacerbating the disincentive to develop next-generation therapies inherent in the Negotiation Program to the point of suffocating all such innovation, to the detriment of patients in need. The sheer breadth of CMS’s “qualifying single source drug” definition—which amalgamates drug products by common active moiety and biological products by common active ingredient—leaves no incentive for therapeutic advancement and will have significant, negative impacts on innovation for years to come.

Biopharmaceutical innovation is incremental, relying on sustained and continuous improvements to molecules, pathways, and modes of administration to achieve maximum clinical benefit for patients. Researchers cannot take significant leaps and develop new active moieties with each generation of treatment. By combining drugs at the active moiety or active ingredient level, CMS is harming investments into new therapies, including for orphan and hard to treat diseases. For the sake of pharmaceutical and biotechnology innovation, and patient access to needed therapies, CMS’s current framework cannot stand.

²⁰ *Green v. Bock Laundry Machine Co.*, 490 U.S. 504, 528 (1989) (Scalia, J., concurring); cf. *Erlenbaugh v. United States*, 409 U.S. 239, 243–44 (1972) (under the rule of *in pari materia*, it is generally “assume[d] that whenever Congress passes a new statute, it acts aware of all previous statutes on the same subject”).

²¹ 21 U.S.C. § 355(a); 42 U.S.C. § 262(a)(1)(A).

²² 21 U.S.C. § 355(c), (d); 21 C.F.R. §§ 314.105, 314.125 (NDA requirements); 42 U.S.C. § 262(a)(2)(C); 21 C.F.R. §§ 601.2(a), 601.4(a) (BLA requirements).

²³ FDA, Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees (Dec. 2004), available at <https://www.fda.gov/media/72397/download>. For example, a new active ingredient (e.g., a different salt, ester, or complex of an approved moiety) should be approved under a new application. *Id.* at 3. In contrast, a new strength generally should be approved under a supplement. *Id.* at 4. The same is true for a new container size or package type of the same indication and route of administration. *Id.* Certain changes in dosage form and route of administration should be approved under a supplement, but others should be approved under a new application. *Id.* at 3.



Second, an application-based framework would create an easily administrable bright line rule based on a familiar standard, to the benefit of both CMS and manufacturers. A bright line rule would enable CMS to more readily identify relevant dosage forms and strengths for purposes of aggregating Medicare expenditures and applying the MFP.²⁴ And a bright line rule would enable manufacturers to more confidently track the seven- or eleven-year “qualifying single source drug” clock, and thereby make more informed decisions about research and development.

For these reasons, BIO strenuously disagrees with CMS’s approach to identifying a qualifying single source drug by reference to common active moiety (drugs) or common active ingredient (biologics). Both law and policy dictate that a qualifying single source drug be identified by reference to its NDA or BLA.

Notably, it necessarily follows from the identification of a qualifying single source drugs by reference to its NDA or BLA that the dosage forms and strengths of such a drug (across which Medicare expenditures are aggregated and the MFP is applied) also must be identified by reference to the NDA or BLA of the drug. With respect to a qualifying single source drug, the statute requires CMS to aggregate Medicare expenditures “us[ing] data that is aggregated across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended release formulation, and not based on the specific formulation or package size or package type of the drug.”²⁵ Similarly, with respect to a qualifying single source drug that is a selected drug, the statute requires CMS to “establish[] . . . procedures to compute and apply the maximum fair prices across different strengths and dosage forms of [the] drug and not based on the specific formulation or package size or package type of such drug.”²⁶ Accordingly, Medicare expenditures are to be aggregated, and the MFP is to be applied, across only dosage forms and strengths of the qualifying single source drug. As set forth above, a qualifying single source drug must be identified by reference to its NDA or BLA; it necessarily follows that the dosage forms and strengths of such a drug also must be identified by reference to the NDA or BLA of the drug.²⁷

It is imperative that CMS immediately rescind the approach set forth in the Initial Guidance—under which Medicare expenditures are aggregated, and the MFP is applied, across dosage forms and

²⁴ See SSA §§ 1192(d)(3)(B), 1196(a)(2).

²⁵ *Id.* § 1192(d)(3)(B) (emphasis added).

²⁶ *Id.* § 1196(a)(2) (emphasis added).

²⁷ The references to “formulations” in the statutory text do not change the analysis. In context, such formulations are plainly limited to formulations of the dosage forms and strengths of the qualifying single source drug. See, e.g., A. Scalia & B. Garner, *Reading law: The interpretation of Legal texts* 199, 203-132–33 (2012) (“[T]he verb to include introduces examples, not an exhaustive list.”). We note that formulations of dosage forms and strengths may be approved under the same NDA or BLA. See FDA, Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees 3–4.



strengths of products that share the same active moiety (drugs) or the same active ingredient (biologics)—and instead specify that, for purposes of aggregation of Medicare expenditures and application of the MFP, dosage forms and strengths are also identified by reference to the NDA or BLA of the qualifying single source drug, consistent with the requirements of the statute.²⁸

C. Orphan drugs

BIO urges CMS to clarify the scope of the orphan drug exclusion in a manner that maximizes protection for orphan drugs.

A drug is categorically ineligible for selection for negotiation if “designated as [an orphan drug] for only one rare disease or condition . . . and . . . the only approved indication (or indications) is for such disease or condition.”²⁹ It is imperative that CMS implement the orphan drug exclusion to be maximally protective of orphan drugs, in recognition of the unique need to maintain incentives for developing new therapies targeting rare diseases.

The Negotiation Program poses special risks to patient populations awaiting the development of new orphan drugs. By definition, orphan drugs target diseases affecting less than 200,000 people in the United States.³⁰ As such, such drugs are particularly susceptible to the chilling effect of factors that discourage research and development. On average, the development of a single drug takes anywhere from ten to fifteen years and costs upwards of \$2.6 billion in research and development³¹—and the development of an orphan drug, often takes even longer and costs even more. Limited patient populations make it inherently more challenging for the developers of orphan drugs to recoup this investment, especially because orphan drug developers are overwhelmingly small emerging companies: Start-ups and emerging biotechnology companies are responsible for fully 85% of all orphan-designated products in development.³²

²⁸ Regardless of the “qualifying single source drug” definition adopted by the Agency, CMS must consistently apply such definition. As such, if CMS were to maintain that products that share the same active moiety (drugs) or the same active ingredient (biologics) are the same qualifying single source drug, BIO agrees that the market entry of a generic or biosimilar to any such product would disqualify all such products from treatment of a qualifying single source drug. See Initial Guidance at 10. Any other approach would be irreconcilable with CMS’s stated “qualifying single source drug” definition. See, e.g., *Nat’l Credit Union Admin. v. First Nat. Bank & Tr. Co.*, 522 U.S. 479, 501–02 (1998) (a basic canon of interpretation is that similar or identical language “be accorded a consistent meaning”).

²⁹ SSA § 1192(e)(3)(A) (such drugs are categorically ineligible for selection for negotiation because they are excluded from the definition of “qualifying single source drug”).

³⁰ See 21 C.F.R. § 316.10(d)(8)(ii).

³¹ T. Sullivan, A Tough Road: Cost to Develop One New Drug Is \$2.6 Billion, Policy & Med., <https://www.policymed.com/2014/12/a-tough-road-cost-to-develop-one-new-drug-is-26-billion-approval-rate-for-drugs-entering-clinical-de.html> (Mar. 21 2019).

³² D. Thomas & C. Wessel, 2019 *Emerging Therapeutic Company Trend Report*, BIO Industry Analysis 40 (2019), available at <http://go.bio.org/rs/490-EHZ-999/images/BIO%202019%20Emerging%20Company%20Trend%20Report.pdf>.



As such, it is vitally important that CMS take special steps to protect development of and access to orphan drugs. The stakes could not be higher for patients. There are over 7,000 known rare diseases, and approximately thirty new ones are identified each year.³³ While each rare disease affects only a relatively small number of patients, collectively, over thirty million Americans are affected by a rare disease, with an estimated cost to society in excess of \$1 trillion annually.³⁴ Further, 95% of rare diseases currently have no approved medical treatment.³⁵ According to a 2020 IQVIA/National Organization for Rare Diseases report examining trends in rare disease innovation, “there are [only] 447 drugs with orphan-only indications, with 104 drugs approved for two or more orphan indications.”³⁶ As such, there is a pressing need to maintain strong incentives for continuing orphan drug development.

Research and development regarding the application of existing therapies to rare diseases is one way to chip away at this disparity. The orphan drug exclusion, however, discourages precisely such scientific discovery. Therefore, as the Agency “consider[s] whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development,”³⁷ BIO urges the Agency to implement, at a minimum, the following recommendations to better support ongoing development of and access to drugs targeting patients living with rare diseases.

First, CMS should establish a process that enables manufacturers to submit evidence that an indication falls within an orphan drug designation to account for situations where CMS is unable to determine eligibility for the orphan drug exclusion based on a review of FDA’s orphan drug databases.

As set forth above, the orphan drug exclusion is based on whether a drug has an orphan drug designation for a single rare disease, and whether its approved indications are for such rare disease.³⁸ In many cases, CMS will be able to readily determine whether a drug meets such

³³ BIO, Rare Diseases & Orphan Drugs, <https://www.bio.org/policy/human-health/rare-diseases-orphan-drugs> (last visited Feb. 28, 2023).

³⁴ S. Garrison, et al., *The Economic Burden of Rare Diseases: Quantifying the Sizeable Collective Burden and Offering Solutions*, Health Affairs Forefront, <https://www.healthaffairs.org/doi/10.1377/forefront.20220128.987667/> (Feb. 1, 2022).

³⁵ Nat’l Insts. of Health, *Delivering Hope for Rare Diseases* 1 (Jan. 2022), available at https://ncats.nih.gov/files/NCATS_RareDiseasesFactSheet.pdf.

³⁶ IQVIA, *Orphan Drugs in the United States* 7 (Dec. 2020), available at <https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/orphan-drugs-in-the-united-states-rare-disease-innovation-and-cost-trends-through-2019/orphan-drugs-in-the-united-states.pdf>.

³⁷ Initial Guidance at 11.

³⁸ SSA § 1192(e)(3)(A).



criteria using publicly available information. This is because FDA maintains various databases containing relevant information.³⁹

But there are situations where an approved indication falls within the scope of an orphan drug designation but there is no corresponding grant of orphan exclusivity.⁴⁰ In such situations, CMS cannot rely on FDA's databases, as the Agency states in the Initial Guidance it will do,⁴¹ to accurately determine eligibility for the orphan drug exclusion—because those databases principally track orphan exclusivity, rather than orphan drug designation.⁴²

To account for such situations, CMS should create a process that enables manufacturer to provide evidence that an indication falls within an orphan drug designation, where such fact is not ascertainable from FDA databases alone. Acceptable evidence should include written communications with FDA, whether pre- or post-approval. CMS should also establish this process as soon as possible, so that manufacturers can work with FDA and otherwise develop evidence that their drugs are eligible for the orphan drug exclusion, well in advance of the first selected drug publication date.

Second, CMS should confirm that it will determine eligibility for the orphan drug exclusion based on orphan drug designation *at the time of selection*.

Under FDA regulations, a manufacturer may voluntarily withdraw a requested or granted orphan drug designation at any time.⁴³ Where a manufacturer does so, the withdrawal is publicized, and any benefits associated with the designation cease.⁴⁴ Accordingly, when determining eligibility for the orphan drug exclusion, CMS should confirm that it will look only to orphan designation at the time of selection, and will not look to any prior designation that has been withdrawn. Doing so would help avoid improperly narrowing the universe of protected orphan drugs.

³⁹ Such databases include FDA's orphan drug designation/exclusivity database, the drugs@FDA database, and the Approved Drug Products with Therapeutic Equivalence Evaluations publication (Orange Book).

⁴⁰ There are various circumstances where this can arise. For instance, it can occur in certain circumstances where an orphan drug is approved for the same indication as a previously approved drug, but is not clinically superior to the previously approved drug. In such a circumstances, although the indication falls within the scope of the orphan designation, it does not qualify for orphan exclusivity.

⁴¹ Initial Guidance at 11.

⁴² Orphan exclusivity is, in itself, irrelevant for purposes of the orphan drug exclusion. The orphan drug exclusion is unambiguously based on whether all indications of a drug with a single orphan drug designation fall within the scope of that designation. It is therefore immaterial whether the drug also has (or had) orphan exclusivity.

⁴³ 21 C.F.R. § 316.24(d).

⁴⁴ *Id.*



Third, CMS should clarify that, where an orphan drug loses eligibility for the orphan drug exclusion, the seven- or eleven-year “qualified single source drug” clock runs from *the date on which the drug lost eligibility for the exclusion*.

Doing so would help maximize protection for orphan drugs. Absent such clarification, an orphan drug that loses eligibility for the orphan drug exclusion could be virtually immediately subject to selection for negotiation, simply because it was designated as an orphan drug for a second rare disease or an indication was approved for a second rare disease. CMS’s implementation of the orphan drug exclusion would thereby disincentivize progress in rare disease drug development, which is often predicated upon identification of promising new uses of existing therapies. CMS should act to avoid such a result, as it would further disincentivize developers of orphan drugs from investing in treatments for a second rare disease.

Implementing the above recommendations is necessary to mitigate the risk that the Negotiation Program will deter the development of orphan drugs to treat those suffering from rare diseases. It is also fully consistent with long-standing Congressional policy favoring protection of orphan drugs. Such policy dates back to the early 1980s, when Congress enacted the Orphan Drug Act of 1983 to create various incentives to encourage and facilitate the development of new orphan drugs.⁴⁵ In keeping with Congress’s long-held policy of protecting orphan drugs, CMS should make every effort to ensure that it does not hamper orphan drug innovation as it implements the Negotiation Program and its orphan drug exclusion.

D. Small biotech drugs

Under the IRA, a drug is exempt from negotiation for initial price applicability years 2026, 2027, and 2028 if spending on the medicine comprises: (1) a small percentage of Medicare program spending, and (2) a significant proportional share of a company’s Medicare business. This is referred to as the Small Biotech Exception. This critical protection recognizes that small biotech manufacturers with a single product that represents the vast majority of their Medicare revenue will be disproportionately impacted by negotiation, which could have an immediate and tangible impact on the ability of such manufacturers to invest in future R&D – and in particular, in areas that predominantly affect the Medicare population.

CMS does not address how or when it will notify manufacturers regarding its determination of whether a drug, based on the information the manufacturer submits through the proposed ICR, qualifies for the Small Biotech Exception. **To that end, our comments that follow focus on ensuring predictability and**

⁴⁵ See Orphan Drug Act, Pub. L. No. 97-414, §§ 1, 2, 96 Stat. 2049, 2049–51 (1983), as amended by Pub. L. 98-551, 98 Stat. 2815, 2817 (1984).



transparency for small biotech manufacturers that apply for the exception. This includes the following process attributes:

- Clear process (i.e., who submits, what to submit, when to submit) for applying for or recertifying a drug qualifies for the Small Biotech Exception.
- Appropriate and fair timelines to submit information to qualify.
- Consistency and clear criteria in evaluating submissions to qualify for the Small Biotech Exception.
- Proper and timely notification regarding qualification if the drug meets the Small Biotech Exception requirements.
- Proper and timely notification if the drug does NOT meet the Small Biotech Exception requirements, as well as a clear dispute process for appeal of such decision.
- Clarity regarding the form and manner that CMS will use to notify manufacturers if they meet – or do not meet – the criteria for the Small Biotech Exception.

Submissions for Initial Price Applicability Year 2026. CMS has indicated that the current Small Biotech Exception ICR is focused only on initial price applicability year 2026. However, as discussed further below, given that the agency has not made publicly available the data on which it will rely with regard to total expenditures for the purpose of determining eligibility for the Small Biotech Exception under section 1192 (d)(2,) or whether a drug meets the test of a high spend drug under section 1192 (d)(1), it is impossible for small biotech manufacturers to make a reasonable inference regarding whether a submission is warranted in the current or future years on the basis of the requisite statutory thresholds. We recommend that any company that believes it qualifies for the Small Biotech Exception under section 1192 (d)(2) should be able to apply and be approved for this exception this year regardless of whether the drug meets the test of a high spend drug under section 1192 (d)(1). This will provide important certainty and predictability for small biotech manufacturers. Such certainty is critical as most small biotech manufacturers have only one or a limited number of products on the market. We also believe the statute contemplates such an approach, as the exception in section 1192 (d)(2)(A) refers to a “qualifying single source drug” that meets either the test in section 1192 (d)(2)(A)(i) or section 1192 (d)(2)(A)(ii), and these tests refer to Medicare expenditures in 2021, and the data for any small biotech company is readily available to CMS. To provide additional predictability and mitigate uncertainty for small biotech manufacturers, CMS should also clearly articulate the specific criteria manufacturers should consider in determining whether to apply for the Small Biotech Exception for initial price applicability year 2026.

Clarity on Process and CMS Response to Small Biotech Manufacturer. CMS should specify not only the timeline for when the submission of information by the small biotech manufacturer is due, but also the timeline for CMS review and response to the manufacturer, in situations where CMS grants the



exception as well as situations where CMS does not. To promote certainty for small biotech manufacturers, CMS should commit to responding to each manufacturer as far in advance of September 1, 2023, as possible.

- *Clear Timelines.* We suggest the following as a timeline that would allow for appropriate transparency, clarity, and completion of the process in advance of the September 1, 2023, publication of drugs selected for negotiation:
 - Submission by small biotech manufacturers due June 10, 2023;
 - CMS response to small biotech company (affirmative or negative) due by June 30, 2023;
 - Small biotech company response to negative determination by July 20, 2023;
 - Final CMS response to small biotech company by August 10, 2023.
- *Clarity on Data Source for 2021 Drug Spending and Availability of Data for Manufacturers.* CMS should clarify what data source it will use for identifying 2021 total expenditures for the qualifying single source drug, as the agency has stated that the drug dashboard data published at [cms.gov](https://www.cms.gov) is not being used for the IRA negotiation provisions; we also understand CMS is considering use of Prescription Drug Event (PDE) data. We recommend that CMS provide the data it will be using for 2021 to manufacturers so that this data can be validated by manufacturers that apply for (or will apply for) the Small Biotech Exception.
- *CMS Response and Justification for Decision.* CMS should provide clarity on the form and content of its expected response and notification to small biotech manufacturers applying for the exception, specifically whether the response will be by letter, email, or other form of official communication. Further, if CMS determines that it does not agree that a small biotech drug qualifies for the exception, CMS's response should outline in sufficient detail how such a determination was made, including on which expenditure data the agency relied and other information, as relevant, that led to a negative determination. Further, CMS should indicate if the rationale for the denial is restricted to initial price applicability year 2026 or all years for which the Small Biotech Exception applies.
- *Dispute Resolution.* CMS should provide a dispute resolution process where the manufacturer can respond to and appeal a negative determination by CMS. Specifically, the small biotech manufacturer should have the opportunity to provide additional data or information to the agency to support its application for the Small Biotech Exception.
- *Flexibility.* Given that this is a new program and process, and that only a limited number of small biotech manufacturers will be providing submissions to CMS, we recommend that the agency allow for a flexible approach. For example, if CMS determines that information submitted by the



small biotech manufacturer is incomplete or unclear, we urge CMS to engage in a dialogue with the manufacturer to resolve any outstanding issues to complete their submission. Further, for the first year of the program, we encourage CMS to allow a small biotech manufacturer to submit information after the information submission deadline, such as in good faith circumstances where a small biotech manufacturer may later realize that it should qualify for the exception.

- *One-time Qualification.* We request that manufacturers should not need to reapply in subsequent years if a drug has previously received the Small Biotech Exception and there is no material change in the manufacturer's circumstances. Manufacturers could submit an attestation that nothing in their application has materially changed from the prior year and if there has been a material change the manufacturer could submit an updated form.
- *Clear Definition of "Acquired."* We recommend CMS include a definition for what it means to be "acquired" pursuant to section 1192(d)(2)(B)(ii). CMS should consider defining an acquisition as the transfer of substantially all assets of the manufacturer. Further, CMS should specify whether the acquiring manufacturer meeting the definition of a specified manufacturer will be determined at the time of acquisition. If the acquisition results in a change in eligibility for the small biotech exemption, an updated form should be submitted.
- *Confidentiality of Proprietary Information, Publication of Drugs Qualifying for Small Biotech Exception.* As with all other aspects of the data submitted under provisions of the IRA, CMS must fully protect the confidentiality of all proprietary information submitted in relation to this ICR. At the same time, CMS should outline its approach for sharing with the public information regarding the small biotech drugs the agency determines qualify for the exception. Further, BIO recommends that CMS publish a summary list of the small biotech drugs and manufacturers that qualified. Such information will be important for understanding the impact of this IRA provision and provide further certainty to small biotech manufacturers. We believe that more detail on



how or why a specific manufacturer's drug qualified as a small biotech drug should only be released if that manufacturer chooses to do so.

II. Selection, and Delayed Selection, for Negotiation

A. Background

For each IPAY, the statute directs CMS to publish a list of the drugs that have been selected for negotiation (under statutorily specified parameters) by February 1 of the year that is two years before such IPAY.⁴⁶

The statute provides for a delay in the selection of a biologic for negotiation where, among other things, CMS finds that a biosimilar is highly likely to come to market within two years of what otherwise would be the selected drug publication date.⁴⁷ A first year of delay is granted if the following criteria are met:

- The biologic otherwise would be an extended-monopoly drug;⁴⁸
- The biosimilar manufacturer requests the delay before what would otherwise be the selected drug publication date;⁴⁹
- The biosimilar manufacturer submits specified information and documents;⁵⁰
- CMS finds that the biosimilar is highly likely to be licensed and market within two years of what otherwise would be the selected drug publication date;⁵¹ and
- Certain disqualifying circumstances are not present.⁵²

A second year of delay is granted if the following criteria are met:

- The biologic otherwise would remain an extended-monopoly drug;⁵³
- The biosimilar manufacturer requests the delay before the date that is one year after what would otherwise be the selected drug publication date;⁵⁴ and
- CMS finds that the biosimilar is highly likely to be licensed and marketed within two years of what otherwise would be the selected drug publication date and that, based on clear and

⁴⁶ SSA §§ 1191(b)(3), 1192(a); *see also id.* § 1191(d)(1) (September 1, 2023, for IPAY 2026).

⁴⁷ *Id.* § 1192(f).

⁴⁸ *Id.* § 1192(f)(1)(A); *see also id.* § 1194(c)(4) (defining "extended-monopoly drug").

⁴⁹ *Id.* § 1192(f)(1)(B)(i)(I).

⁵⁰ *Id.* § 1192(f)(1)(B)(ii).

⁵¹ *Id.* § 1192(f)(2)(A).

⁵² *Id.* § 1192(f)(2)(D)(iii), (iv).

⁵³ *Id.* § 1192(f)(2)(D)(ii).

⁵⁴ *Id.* § 1192(f)(1)(B)(i)(II).



convincing evidence, the biosimilar manufacturer has made substantial progress toward licensure and marketing;⁵⁵ and

- Certain disqualifying circumstances are not present.⁵⁶

Where a second year of delay is not granted or the biosimilar does not come to market within two years of what otherwise would be the selected drug publication date, the biologic is selected for negotiation, and the biologic manufacturer must pay a specified rebate.⁵⁷

B. Pre-selection process

Well in advance of the selected drug publication date, CMS should notify each manufacturer of each drug that it intends to select for negotiation and afford each such manufacturer a reasonable opportunity to dispute the propriety of each such intended selection.

The process for selecting a drug for negotiation is complex. Eligibility for selection is based on multiple factors, including whether a sufficient number of years have elapsed since approval or licensure;⁵⁸ whether a generic or biosimilar has come to market;⁵⁹ whether the drug is eligible for the orphan drug exclusion;⁶⁰ whether the drug is a plasma-derived product;⁶¹ whether the drug is a small biotech drug;⁶² whether Medicare expenditures are sufficiently low to disqualify the drug from selection;⁶³ and whether Medicare expenditures are sufficiently high to qualify the drug for selection.⁶⁴

The intricate nature of the selection process presents an inherent risk of a selection error. Notably, if a selection error were identified after the selected drug publication date, CMS would de-select the erroneously selected drug but could not select a substitute. By statute, for a given IPAY, all drugs must be selected by February 1 of the year that is two years before the IPAY.⁶⁵

CMS can readily mitigate this concern by adopting a process for soliciting feedback from manufacturers of potential selected drugs before the selected drug publication date. Specifically, CMS should provide notice to each such manufacturer at least thirty days in advance of the selected drug publication date.

⁵⁵ *Id.* § 1192(f)(2)(B)(i), (iii).

⁵⁶ *Id.* § 1192(f)(2)(D)(iii), (iv).

⁵⁷ *Id.* § 1192(f)(2)(B)(ii), (C).

⁵⁸ *Id.* § 1192(e)(1).

⁵⁹ *Id.*

⁶⁰ *Id.* § 1192(e)(3)(A).

⁶¹ *Id.* § 1192(e)(3)(C).

⁶² *Id.* § 1192(d)(2).

⁶³ *Id.* § 1192(e)(3)(B).

⁶⁴ *Id.* § 1192(d)(1).

⁶⁵ *Id.* §§ 1192(e), 1192(a); see also *id.* § 1191(d)(1) (September 1, 2023, for IPAY 2026).



CMS should then afford the manufacturer at least fourteen days to identify to the Agency any basis on which the manufacturer believes the drug is not, in fact, eligible for selection. Such a pre-selection process would serve an important role in identifying selection errors and further the Agency's interests in transparency, efficiency, and informed decision-making.

In addition to providing advance notice to each manufacturer of a drug that the Agency intends to select, CMS should provide advance notice to each manufacturer of at least each of the next five drugs that would be selected if one or more drugs that the Agency intends to select were found to be ineligible for selection. Doing so would promote efficiency by giving each such manufacturer the same opportunity to engage with the Agency regarding potential selection errors. And doing so would impose no additional burden on the Agency because CMS is already required to identify the top fifty qualifying single source drugs by Part D expenditures and, starting with IPAY 2028, the top fifty qualifying single source drugs by Part B expenditures.⁶⁶

In addition, in advance of the deadline by which a biosimilar manufacturer must request a delay in the selection of a reference biologic for negotiation, CMS should enable such biosimilar manufacturer to ascertain whether the reference biologic is among the drugs that the Agency intends to select (or one of at least the next five drugs in line for selection).

As set forth above, a biosimilar manufacturer may request a delay in the selection of a reference biologic for negotiation.⁶⁷ By statute, such a request must be submitted before the selected drug publication date.⁶⁸ This requirement results in a fundamental timing conundrum: A biosimilar manufacturer will not know whether it should request a delay until after the deadline for requesting the delays has passed.

CMS tacitly acknowledges this timing conundrum in the Initial Guidance but fails to meaningfully address it. The Initial Guidance provides only that a biosimilar manufacturer that “think[s]” that a reference biologic “may” be selected for negotiation should submit a delay request.⁶⁹ This approach is inadequate. Requiring a biosimilar manufacturer to guess whether to submit a delay request is deeply inefficient and unreasonable; just as “[i]t is one thing to expect regulated parties to conform their conduct to an agency’s [actions] once the agency announces them; it is quite another to require regulated parties to divine the agency’s [actions] in advance.”⁷⁰

⁶⁶ See *id.* § 1192(d)(1).

⁶⁷ *Id.* § 1192(f).

⁶⁸ *Id.* § 1192(f)(1)(B)(i).

⁶⁹ Initial Guidance at 16.

⁷⁰ *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 158–59 (2012).



To make the delay request provision meaningful, it is essential that CMS instead create a way for a biosimilar manufacturer, with appropriate confidentiality safeguards, to ascertain whether a reference biologic is likely to be selected before the delay request submission deadline. CMS should enable a biosimilar manufacturer to inquire with the Agency starting at least thirty days in advance of such deadline.

C. Delayed selection of a biologic for negotiation on account of anticipated biosimilar market entry

As set forth below, BIO makes a number of recommendations to enhance the implementation of the process by which a biosimilar manufacturers may request a delay in the selection of a reference product for negotiation.

As set forth above, the statute directs CMS to delay the selection of a biologic for negotiation under specified circumstances.⁷¹ BIO makes the following recommendations to enhance the implementation of the delay process:

First, it is vital that CMS afford a biosimilar manufacturer a *meaningful* opportunity to request a delay, reset the delay request submission deadline closer to the selected drug publication date and permit broad supplementation of a timely request.

If CMS does not adopt these recommendations, it will undermine the fidelity of the information on which it relies in making a “high likelihood” determination—and indeed Congress’s objective in providing for a delay request.

With respect to the timing of a delay request, under the Initial Guidance, a biosimilar manufacturer must give notice of its intent to submit a delay request by May 10, 2023.⁷² CMS will then provide a fillable template to complete and access to a Box folder within five business days, i.e., by May 17, 2023.⁷³ The manufacturer must then upload a completed templated and all supporting documentation by May 22, 2023—only three business days later, yet over three months in advance of the selected drug publication date.⁷⁴ There is no justification for such an extraordinarily and needlessly truncated window of time in which to submit a multifactorial request—a concern that is only compounded by CMS’s policy of automatically denying an

⁷¹ SSA § 1192(f).

⁷² Initial Guidance at 21.

⁷³ *Id.*

⁷⁴ *Id.*



incomplete request.⁷⁵ Indeed, such timing constraint works to defeat the Congressional objective in providing for a delay request: By effectively eliminating the additional runway for a biosimilar competitor to come to market, it acts as a barrier to the biosimilar competition that Congress sought to nurture. It is imperative that CMS afford a biosimilar manufacturer a meaningful opportunity to request a delay.

In addition, to ensure that CMS adjudicates a delay request based on the most mature information possible, CMS should (1) set the delay request submission deadline as close as reasonably possible to the selected drug publication date and (2) permit broad supplementation of a timely request with late-breaking information or otherwise for good cause. As noted above, under the Initial Guidance, a biosimilar manufacturer must give notice of its intent to submit a delay request by May 10, 2023—over three months in advance of the selected drug publication date.⁷⁶ And CMS will permit supplementation by the biosimilar manufacturer, beyond supplementation requested by the Agency, only with respect to whether the BLA has been accepted or approved by FDA.⁷⁷

Information bearing on the expected timing of licensure and marketing often rapidly changes. The expected timing of market entry can fluctuate based on a range of factors, including FDA communications regarding the BLA and changes to the manufacturer’s production or distribution arrangements. In order for CMS to make an informed determination regarding eligibility for delayed selection, it is vitally important that the Agency rely on all of the most recent available information that bears on the likelihood of market entry within the requisite time period.

An accurate “high likelihood” determination also reduces administrative burden. If CMS makes an erroneous determination based on outdated or incomplete information, the Agency will be required to administer the payment of a rebate by the reference biologic manufacturer. Such needless inefficiency can be avoided by enabling the Agency to rely on the most recent available information by (1) setting the delay request submission deadline as close as reasonably possible to the selected drug publication date and (2) permitting broad supplementation of a timely request with late-breaking information or otherwise for good cause.

Second, CMS should provide notice of its delay request determination in advance of the selected drug publication date and establish a dispute resolution process.

⁷⁵ *Id.* at 22.

⁷⁶ *Id.* at 21.

⁷⁷ *Id.* at 23.



Under the Initial Guidance, CMS will not inform a biosimilar manufacturer of an unsuccessful delay request until after the selected drug publication date.⁷⁸ This effectively means that the biosimilar manufacturer will have no opportunity to dispute the determination.

The Agency instead should provide notice of an unsuccessful delay request in advance of the selected drug publication date and establish a process by which the biosimilar manufacturer can dispute an erroneous determination. BIO recommends that CMS provide such notice at least fourteen days in advance of the selected drug publication date and afford the biosimilar manufacturer at least seven days to dispute the determination.

Third, CMS should accept and consider all information that the biosimilar manufacturer determines relevant to determining eligibility for delayed selection.⁷⁹

As noted above, there are countless factors that can affect the expected timing of licensure and approval. It follows that CMS should not artificially limit the information that it considers in determining eligibility for delayed selection. Accordingly, it is vital that CMS enable the biosimilar manufacturer—the party closest to the information—to submit all information that it determines relevant to the delay request.⁸⁰

There is clear statutory authority to enable the biosimilar manufacturer to submit such information. The statute provides that the biosimilar manufacturer must submit “information and documents necessary for [CMS] to make [the delayed selection determination], as specified by [CMS]”⁸¹ In addition, the statute provides that, after CMS has reviewed the delay request, the biosimilar manufacturer must submit “any additional information and documents requested by [CMS] necessary to make [the delayed selection determination].”⁸²

CMS therefore has broad discretion in specifying what the biosimilar manufacturer must submit in support of the delay request. The Agency should exercise such discretion and request that the manufacturer submit all relevant information. Doing so would help ensure that CMS has the most pertinent information before it, as the biosimilar manufacturer is the entity best situated to identify the information that bears on the delay request.

⁷⁸ *Id.* at 24.

⁷⁹ See SSA § 1192(f)(1)(B)(ii)(I)(aa) (“information and documents necessary for the Secretary to make determinations under this subsection, as specified by the Secretary”), (II) (“additional information and documents requested by the Secretary necessary to make determinations under this subsection”).

⁸⁰ In the Initial Guidance, CMS enables the submission of only the statutory minimum information. Initial Guidance at 22.

⁸¹ SSA § 1192(f)(1)(B)(ii)(II). The statute goes on to specify that such information “includ[es]” the information specified in section 1192(f)(1)(B)(ii)(III). *Id.*

⁸² *Id.* § 1192(f)(1)(B)(ii)(II).



Notably, CMS also has clear legal authority to consider all such information in making a “high likelihood” determination.

Section 1192(f)(3) sets forth a set of circumstances under which CMS must find a high likelihood of timely market entry—based on a limited set of enumerated information and documents, including information and documents described in section 1192(f)(1)(B)(ii)(III) (subclause (III)).⁸³ Critically, section 1192(f)(3) cannot be interpreted to set forth the only set of circumstances under which CMS may find a high likelihood of timely market entry.

The broader structure of section 1192(f) makes clear that Congress intended that the full range of relevant information and documents be considered by CMS, not only the limited set of information and documents enumerated in section 1192(f)(3). This is because section 1192(f)(1)(B)(ii)(I)(aa) (subclause (I)(aa)) clearly requires the biosimilar manufacturer to submit information and documents necessary to rendering the “high likelihood” determination—“includ[ing]” (but not limited to) the information and documents described in subclause (III).

The necessary implication is that there are information and documents beyond the information and documents described in subclause (III)—which are also “necessary” to rendering the “high likelihood” determination. While the information and documents described in subclause (III) are accounted for in section 1192(f)(3), the remaining information and documents described in subclause (I)(aa) are not—despite being “necessary” to rendering the “high likelihood” determination. Thus, if section 1192(f)(3) were the only set of circumstances under which CMS may find a high likelihood of timely market entry, the language in subclause (I)(aa) requiring broad submission of pertinent information and documents beyond those in subclause (III) would be rendered a nullity.⁸⁴ Because the information and documents described in subclause (I)(aa) serve no other statutory purpose, the only way to give meaning to the entirety of subclause (I)(aa) is to assign it its most natural meaning: Information and documents described in subclause (I)(aa) are “necessary” to rendering the “high likelihood” determination and, thus, CMS may consider all such information and documents submitted in rendering such determination. Accordingly, section 1192(f)(3) does not set forth the only set of circumstances under which CMS may find a high likelihood of timely market entry.

There is every reason to think that Congress intended for CMS to consider all relevant evidence in rendering the “high likelihood” determination. Any other interpretation of the statute would

⁸³ *Id.* § 1192(f)(3).

⁸⁴ See *Duncan v. Walker*, 533 U.S. 167, 175 (2001) (a statute is not to be interpreted in a manner that renders any provision a nullity or otherwise meaningless).



yield an absurd result. Through subclause (I)(aa), Congress clearly granted CMS broad discretion to identify and collect information and documents “necessary” to rendering the determination. If CMS were to refuse to consider such information, it would be tantamount to the Agency acknowledging that it is rendering the determination without considering information and documents that the Agency itself has concluded is essential to doing so. It is hard to imagine more arbitrary and capricious governmental decision-making.⁸⁵ Accordingly, CMS should request all information that a biosimilar manufacturer concludes supports a “high likelihood” determination and consider all such information in rendering such determination.

Fourth, we appreciate CMS’s confirmation that an agreement between a biosimilar manufacturer and a reference biologic manufacturer that permits the biosimilar manufacturer to market the biosimilar is not necessarily an agreement that incentivizes the biosimilar manufacturer to request a delay. But we ask for clarification on the circumstances under which CMS will find a disqualifying agreement to exist.

The statute provides that a delay request may not be granted where, based on specified information,⁸⁶ a biosimilar manufacturer and a reference biologic manufacturer have entered into an agreement that incentivizes (or requires) the biosimilar manufacturer to request a delay.⁸⁷ In the Initial Guidance, CMS correctly acknowledges that an agreement between a biosimilar manufacturer and a reference biologic manufacturer “that permits the Biosimilar Manufacturer to [timely] market the Biosimilar in one or more dosage form(s), strength(s), and indication(s)” not only is not necessarily an agreement that incentivizes the biosimilar manufacturer to request a delay but indeed can be a form of clear and convincing evidence of a high likelihood of timely market entry.⁸⁸ It would be contrary to the statute for CMS to suggest otherwise. This is because the statute clearly directs CMS to consider agreements between the biosimilar manufacturer and the reference biologic manufacturer in rendering the delayed selection determination.⁸⁹ It would nullify this statutory instruction if the mere existence of an agreement between the biosimilar manufacturer and the reference biologic manufacturer were automatically disqualifying. It is well understood that a statute should not be interpreted in a manner that renders text meaningless or otherwise nugatory.⁹⁰

⁸⁵ See 5 U.S.C. § 706(2)(A).

⁸⁶ SSA § 1192(f)(1)(B)(ii)(I)(bb) (“all agreements related to the biosimilar biological product filed with the Federal Trade Commission or the [Department of Justice] pursuant to subsections (a) and (c) of section 1112 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003,” which include agreements between “brand name drug companies” and “generic drug applicants”).

⁸⁷ *Id.* § 1192(f)(2)(D)(iv).

⁸⁸ Initial Guidance at 19.

⁸⁹ SSA § 1192(f)(1)(B)(ii)(I)(bb), (2)(B)(i)(II), (3)(B).

⁹⁰ *United States v. DBB, Inc.*, 180 F.3d 1277, 1285 (11th Cir. 1999) (“A statute should be ‘interpreted so that no words shall be discarded as meaningless, redundant, or mere surplusage.’”) (internal citations omitted).



BIO, however, asks CMS to clarify the circumstances under which the Agency will find a disqualifying agreement to exist. In the Initial Guidance, CMS states only that an agreement may not “impos[e] improper constraints on the Biosimilar Manufacturer.”⁹¹ Yet, despite the absence of meaningful guidance regarding such constraints, CMS will require a biosimilar manufacturer requesting a delay to certify that it has not entered into a disqualifying agreement,⁹² on pain of potential “liability, including under the False Claims Act.”⁹³ To promote market certainty by enabling manufacturers to more confidently make more informed decisions about the arrangements into which they enter, it is imperative that CMS clarify what constitutes an agreement that incentivizes a biosimilar manufacturer to request a delay.

III. Negotiation Process

A. Background

The statute requires CMS to “develop and use a consistent methodology and process” to negotiate the MFP.⁹⁴ In addition, the statute requires the manufacturer to submit specified information by March 1 of the year that is two years before the applicable IPAY.⁹⁵ CMS must make a written initial offer by June 1, which must include a concise justification that considers certain statutorily enumerated negotiation factors.⁹⁶ Within thirty days of receipt, the manufacturer must accept the initial offer or make a written counteroffer, which must include a justification that considers the same statutorily enumerated negotiation factors.⁹⁷ CMS must respond in writing to any counteroffer,⁹⁸ and the negotiation period must end by November 1.⁹⁹

⁹¹ Initial Guidance at 19.

⁹² *Id.* at 77.

⁹³ *Id.* at 80.

⁹⁴ SSA § 1194(b)(1). The renegotiation process must be consistent with the negotiation process to the extent practicable. *Id.* § 1194(f)(1), (4).

⁹⁵ *Id.* §§ 1194(b)(2)(A), (e)(1), 1194(a)(4); *see also id.* § 1191(d)(5)(A) (October 2, 2023, for IPAY 2026).

⁹⁶ *Id.* § 1194(b)(2)(B); *see also id.* § 1191(d)(5)(B) (February 1, 2024, for IPAY 2026).

⁹⁷ *Id.* § 1194(b)(2)(C).

⁹⁸ *Id.* § 1194(b)(2)(D).

⁹⁹ *Id.* § 1194(b)(2)(E); *see also id.* § 1191(d)(5)(C) (August 1, 2024, for IPAY 2026).



B. Negotiation process

BIO asks CMS to adopt its recommendations to improve the proposed negotiation process.

As noted above, the statute mandates that CMS “develop and use a consistent methodology and process” for MFP negotiation.¹⁰⁰ Thus, Congress intended for the negotiation process to be transparent to and predictable for all parties. Although no two negotiations will ever be identical—because the circumstances of each selected drug are unique—all negotiations should be subject to a clear and reasonable framework. A consistent process not only is statutorily required but also helps to ensure that CMS complies with its obligation to treat similarly situated entities in a similar manner, absent a reasoned basis for distinction.¹⁰¹

The Initial Guidance proposes that, only where CMS rejects a counteroffer, the Agency will extend an invitation for a negotiation meeting to take place within thirty days of receipt of such counteroffer.¹⁰² CMS would hold a maximum of three such meetings: an initial meeting and up to one additional meeting at the request of either CMS or the manufacturer.¹⁰³ The Initial Guidance also proposes to allow the parties to discuss new information during such meetings.¹⁰⁴

With respect to justifying an initial offer, the Initial Guidance only recites the statutory requirement of a concise justification based on the statutorily enumerated negotiation factors.¹⁰⁵ The Initial Guidance is silent as to any justification of a response to a counteroffer.

BIO makes the following recommendations to improve the proposed negotiation process:

First, CMS should further enable a negotiation process that allows for meaningful engagement and dialogue between CMS and manufacturers. BIO appreciates that CMS’s recognition that real dialogue (as opposed to a paper-based process) is essential to fulfilling Congress’s intent in establishing a “Negotiation” Program with a mandated process “for negotiations,”¹⁰⁶ which necessarily contemplates meaningful engagement between the Agency and the manufacturer on the unique circumstances presented by each selected drug.¹⁰⁷

¹⁰⁰ *Id.* § 1194(b)(1).

¹⁰¹ *See Bracco Diagnostics*, 963 F. Supp. at 27–28.

¹⁰² Initial Guidance at 55.

¹⁰³ *Id.* at 55–56.

¹⁰⁴ *Id.* at 56.

¹⁰⁵ *Id.* at 54.

¹⁰⁶ SSA § 1194(b)(1).

¹⁰⁷ *See Wheeler v. St. Joseph Hosp.*, 133 Cal. Rptr. 775, 790 (Ct. App. 1976) (differentiating between “negotiated contracts” and contracts of adhesion).



BIO, however, is concerned that the agency is arbitrarily limiting such engagement to (1) the period after the rejection of a counteroffer and (2) a maximum of three meetings. There is no logical reason for such limitations, as (1) such engagement can equally inform an initial offer, potentially sparing the parties the need to consider a counteroffer, and (2) the parties may agree that one or more additional meetings would be helpful and productive in setting the MFP. Accordingly, BIO encourages CMS to revise its proposed negotiation process to (1) enable real dialogue between the parties throughout the negotiation process and (2) specify that, where CMS rejects a counteroffer, additional meetings, beyond those proposed by CMS, may be held without limit where both parties agree to them. We note that such modifications to the negotiation process would be readily manageable given the limited number of drugs subject to such negotiation in any given year.¹⁰⁸

Second, the manufacturer should more generally be permitted to supplement its timely submission where a post-submission development arises or there otherwise is good cause. As set forth above, the statute requires the manufacturer to submit specified information by March 1 of the year that is two years before the applicable IPAY. Inevitably, there will be situations where information relevant to the negotiation arises after the submission deadline has passed. Such late-breaking developments will often be completely unforeseeable at the time of submission but highly relevant to the setting of the MFP. The potential scenarios are virtually limitless: For example, new therapeutic alternatives may come to market; production costs may shift due to ingredient shortages or supply chain issues; or new comparative effectiveness studies may become available.

BIO acknowledges CMS's recognition that it should not blind itself to highly pertinent new information, simply because the submission deadline has passed. But the Agency proposes to limit the presentation of such information to the negotiation meetings during the period after the rejection of a counteroffer. Because such information can equally inform an initial offer, potentially sparing the parties the need to consider a counteroffer, the Agency should more generally permit the manufacturer to supplement its timely submission wherever there is good cause to do so, including when new information relevant to the negotiation process becomes available after the submission deadline.

Permitting supplemental submissions is well warranted. Under the statute, manufacturers are given only one month to prepare a voluminous submission of complex information, including information regarding Non-Federal average manufacturer price (Non-FAMP); research and

¹⁰⁸ See SSA § 1192(a).



development costs; production and distribution costs; federal financial support for discovery and development; pending and approved patent applications, FDA exclusivities, NDAs or BLAs and approvals thereof, market data; and revenue and sales volume data.¹⁰⁹ In some cases, requested data may also not exist in a format required by CMS, such that the manufacturer will need to painstakingly convert raw data from multiple sources into such a format. Manufacturers will assuredly work with utmost diligence to comply with CMS's submission requirements. Still, they may need the flexibility of a supplement to their timely submission for legitimate reasons.

Ultimately, more generally permitting the manufacturer to supplement its timely submission where there is good cause would help ensure that the MFP is set based on the best available information.

Third, CMS should provide a *meaningful* justification of its initial offer and its response to any counteroffer and afford the manufacturer a meaningful opportunity to comment on the response the MFP is set.

As noted above, Congress intended for the MFP to be set via “negotiation,” meaning a bilateral “discussion or process of treaty” between the parties “aimed at reaching an agreement about a particular issue.”¹¹⁰ As with any good faith negotiation, open dialogue will be vital to the success of the MFP negotiation. To this end, BIO asks CMS to specify that its initial offers and its responses to any counteroffers include *meaningful* explanations of how the Agency arrived at the offer or response, including by explaining how the offer or response is supported by the statutorily enumerated negotiation factors and any other information upon which the Agency relied, and how the Agency considered and weighted such factors and information.

As noted above, in the Initial Guidance, CMS states only that the Agency's justification for an initial offer will be “based on” its analysis of statutorily enumerated negotiation factors, but it does not commit to disclosing the details of such analysis.¹¹¹ The Agency does not commit to providing any justification for a response to a counteroffer or an explanation of how it arrived at such response.¹¹²

¹⁰⁹ *Id.* §§ 1193(a)(4), 1194(e)(1).

¹¹⁰ Oxford English Dictionary, Definition of Negotiation, <https://www.oed.com/view/Entry/125879?redirectedFrom=negotiation#eid> (last visited Mar. 2, 2023).

¹¹¹ Initial Guidance at 54.

¹¹² *See id.* at 56–57.



Fully disclosing the bases of both offers and responses to counteroffers would facilitate a more robust—and ultimately more effective—negotiation process. By providing the manufacturer with a meaningful justification for an offer or response, CMS would provide greater opportunity for bilateral dialogue, which would result in more informed and targeted discussions.

BIO also asks CMS to commit to responding to any counteroffer within thirty days. We further ask CMS to commit to affording the manufacturer at least thirty days to comment on the response and considering any such comment before the MFP is set.

This basic procedural protection is essential. Not only would it be consistent with the Agency’s stated interest in “prioritiz[ing] transparency and robust engagement,”¹¹³ but it would also result in more informed and accurate decision-making. It would help prevent the MFP from being set based on an error, a misunderstanding, or a gap in information.

There is ample time in the negotiation schedule for such procedural protection. By statute, an initial offer is made by June 1 (February 1, 2024, for IPAY 2026).¹¹⁴ A counteroffer is made within thirty days of receipt.¹¹⁵ Even if CMS were to wait until June 1 (February 1, 2024, for IPAY 2026) to make the initial offer, and even if the manufacturer were to wait until the thirtieth day after receipt make the counteroffer, there would still be four months remaining in the negotiation schedule (five months for IPAY 2026). Thus, there would be ample time for the recommended additional process.

C. Confidential commercial information

BIO acknowledges CMS’s stated commitment to confidentiality, but recommends that CMS establish more fulsome safeguards to ensure that the Agency is adequately protecting the confidentiality of all proprietary information submitted to CMS as part of the negotiation process. In addition, BIO opposes CMS’s proposed imposition of overly broad confidentiality obligations on manufacturers.

The statute imposes a clear confidentiality requirement: “Information submitted to . . . [CMS] . . . by a manufacturer of a selected drug that is proprietary information of such manufacturer (as determined by . . . [CMS]) shall be used only by . . . [CMS] or disclosed to and used by the Comptroller General of the United States for purposes of carrying out [the Negotiation Program].”¹¹⁶ Congress imposed this

¹¹³ CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026 at 1 (Jan. 1, 2023), available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf>.

¹¹⁴ SSA § 1191(d)(5)(A).

¹¹⁵ *Id.* § 1194(b)(2)(B).

¹¹⁶ *Id.* § 1193(c).



confidentiality requirement for good reason. The statute mandates that manufacturers of selected drugs submit highly sensitive information as part of the negotiation process—including, among other things, information regarding Non-FAMP, research and development costs, production and distribution costs, and revenue and sales volume data.¹¹⁷ It would be deeply disruptive to commercial markets if such proprietary information were disclosed or used in violation of the confidentiality requirement. Indeed, the Initial Guidance acknowledges the “highly sensitive” nature of information to be submitted under the program.¹¹⁸ In principle, BIO is therefore encouraged that CMS states that it “intends to implement a confidentiality policy that is consistent with existing requirements for protecting proprietary information, such as Exemption 4 of [the Freedom of Information Act (FOIA)].”¹¹⁹ That said, there is a pressing need for more detailed specification as to how the Agency will safeguard confidential commercial information to ensure that the statute’s robust confidentiality requirement is fully honored.

BIO therefore asks CMS to more fully specify the controls and safeguards that it will implement. We urge CMS to ensure that such controls and safeguards maximize the protection of confidential commercial information to be submitted under the program. This would be fully consistent with the approach taken in other areas of federal law and policy, which have long given special consideration to such highly sensitive information. For nearly forty years, the Supreme Court has made clear that commercial trade secrets are a “property right [] protected by the Taking Clause of the Fifth Amendment.”¹²⁰ Likewise, Congress has repeatedly made clear its expectation that commercially sensitive information be appropriately safeguarded. For example, even beyond FOIA’s long-standing protection of “trade secrets and commercial or financial information that is obtained from a person and is privileged or confidential,”¹²¹ the Defend Trade Secrets Act prohibits the “misappropriation” of trade secrets through public disclosure and established a private cause of action to enable affected parties to sanction such misappropriation.¹²²

BIO recommends the following minimum controls and safeguards to give full meaning to the confidentiality requirement:

First, CMS should confirm that, in “implement[ing] a confidentiality policy that is consistent with existing requirements for protecting proprietary information,”¹²³ it will ensure protections comparable to, not only those under FOIA, but also those under government price reporting law and policy.

¹¹⁷ *Id.* §§ 1193(a)(4), 1194(e)(1).

¹¹⁸ Initial Guidance at 29.

¹¹⁹ *Id.*

¹²⁰ *Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 1004 (1984).

¹²¹ 5 U.S.C § 552(b)(4); 45 C.F.R. § 5.31(d).

¹²² 18 U.S.C. § 1839(5)(B)(ii)(II).

¹²³ Initial Guidance at 29.



We appreciate CMS’s confirmation that the protections under FOIA, including the prohibition on disclosure of information designated as confidential without providing a pre-disclosure notification and an opportunity to raise objections to disclosure,¹²⁴ will apply to information to be submitted under the program.¹²⁵ We seek confirmation that the protections under government price reporting law and policy will also apply.

In developing the Negotiation Program, Congress did not intend to disrupt the confidentiality requirements under other federal law and policy.¹²⁶ CMS’s confidentiality policy should thus maintain the confidentiality of information protected against disclosure under all other federal law and policy. For example, under MDRP, “information disclosed by manufacturers . . . under [MDRP] . . . is confidential and shall not be disclosed by [CMS] . . . in a form which discloses the identity of a specific manufacturer . . . [or] prices charged for drugs by such manufacturer”¹²⁷ Similarly, Medicare Act provides that “[Average Sales Price (ASP)] information disclosed by manufacturers . . . is confidential and shall not be disclosed by [CMS] in a form which discloses the identity of a specific manufacturer . . . or prices charged for drugs or biologicals by such manufacturer”¹²⁸ Likewise, the 340B Drug Pricing Program (340B Program) generally prohibits disclosures of information submitted by manufacturers under the program.¹²⁹ Where confidential commercial information is protected against disclosure under these or any other federal programs, CMS should safeguard such information against disclosure to at least the same extent.

Second, CMS should implement robust storage and access controls and safeguards to protect the confidentiality of sensitive information. Confidentiality requirements are only as meaningful as the data privacy and security protections that are implemented to safeguard sensitive information against inadvertent or malicious¹³⁰ improper disclosure. Accordingly, CMS should implement robust systems and protocols, including by ensuring that all proprietary information stored in the Health Plan Management System (HPMS) and in electronic

¹²⁴ See 45 C.F.R. §§ 5.41, 5.42.

¹²⁵ Initial Guidance at 29.

¹²⁶ See *Nat’l Ass’n of Home Builders v. Defs. of Wildlife*, 551 U.S. 644, 662 2d 467 (2007) (“[R]epeals by implication are not favored” and will not be presumed unless the “intention of the legislature to repeal [is] clear and manifest.”).

¹²⁷ SSA § 1927(b)(3)(D) (subject to certain limited exceptions).

¹²⁸ *Id.* § 1847A(f)(2)(D) (subject to certain limited exceptions).

¹²⁹ Health Res. & Servs. Admin., General Instructions for Completing the Pharmaceutical Pricing Agreement 7 (2019), available at www.hrsa.gov/sites/default/files/hrsa/opa/pharmaceutical-pricing-agreement-example.pdf.

¹³⁰ Malicious third-party cyber activities have increasingly targeted the federal government—in, part, because its databases are repositories of significant amounts of sensitive information. Cf. David E. Sanger, *Russian Hackers Broke into Federal Agencies, U.S. Officials Suspect*, N.Y. Times, <https://www.nytimes.com/2020/12/13/us/politics/russian-hackers-us-government-treasury-commerce.html> (last updated May 10, 2021).



communications with the Agency is secure and accessible only to CMS staff and only where there is a legitimate programmatic need for access to such information.

In doing so, CMS should look to the safeguards it has already establish under MDRP. Under MDRP, CMS has implemented a system with numerous privacy and security protections to safeguard sensitive product and pricing data submitted by manufacturers. For example, the online interface allows a manufacturer to view its pricing data, such as its Baseline Average Manufacturer Price (AMP) data, while disallowing states, which do not have a programmatic need to view such information, from doing likewise.¹³¹ CMS should ensure that similar controls are in place with respect to HPMS, given CMS's intent to transition most information submissions to that system.

CMS should also specify how it will maintain the confidentiality of the subset of information that is required to be submitted via e-mail or Box. With respect to e-mail, CMS should explain, among other things, how it will enforce access security controls. With regard to Box (a third-party commercial platform), BIO asks CMS to specify how submitted information will be kept confidential, including as against misuse by Box personnel.

Third, CMS should establish a process to enable manufacturers to review a draft of the explanation of the MFP in advance of its publication and raise concerns about disclosure of confidential information. By statute, CMS is required to publish an explanation of the MFP.¹³² Such publication inherently poses heightened risk of disclosure of confidential commercial information. BIO appreciates that CMS intends to make only high-level comments regarding submitted data and refrain from sharing proprietary information.¹³³ But this is insufficient to safeguard against inadvertent disclosure of confidential commercial information. Accordingly, BIO asks that the manufacturer be given an opportunity to review the intended explanation in advance of publication, as well as an opportunity to raise concerns. Such precaution is well warranted here, given Congress's special emphasis on the need for safeguards with respect to the public explanation of the MFP, as evidenced by its specific cross-reference to the statute's confidentiality requirement.¹³⁴

BIO opposes CMS's proposed imposition of overly broad confidentiality obligations on manufacturers. BIO urges CMS to eliminate the proposed, one-sided requirement that manufacturers destroy all records related to the negotiation process and submit a Certificate of Data Destruction to CMS certifying that all

¹³¹ CMS, *Medicaid Drug Programs User Manual 1* (Nov. 3, 2021).

¹³² SSA § 1195(a)(2).

¹³³ Initial Guidance at 29.

¹³⁴ SSA § 1195(a)(2); see also *id.* § 1193(c).



information received from CMS during the negotiation period and potential renegotiation period(s) was destroyed. Like CMS, manufacturers are responsible for maintaining records associated with material decisions and must do so to maintain proper and adequate lines of supervision and oversight by boards, shareholders, and other stakeholders. Manufacturers must therefore be permitted to maintain (in a confidential format) reasonable records associated with the negotiation process to meet their oversight obligations, just as CMS will be maintaining its own records from the negotiation process.

Further, basic due process mandates that manufacturers be given the ability to maintain records related to negotiation proceedings. As CMS knows, the statute contemplates penalties of up to \$1 million per day for failing to submit required information. CMS's Initial Guidance further specifies that the Agency will consider a manufacturer that knowingly submits false information to have violated this provision. Especially given the vast magnitude of such penalties, it is imperative that manufacturers be permitted to maintain complete records of all information they believe may be relevant to defending against the erroneous imposition of sanctions.

It would be troubling in the extreme if manufacturers were required by CMS to destroy the very records that could one day be needed to defend against penalties that could reach hundreds of millions of dollars. "[T]he essence of due process is fundamental fairness," and little could be more fundamentally unfair than mandating destruction of the very records needed to verify an entity's innocence as against erroneous enforcement.¹³⁵

Moreover, BIO takes issue with the more specific blanket prohibition on manufacturers from disclosing or otherwise publicizing information "in the initial offer, including the ceiling price, or the concise justification from the Secretary or any subsequent offer of concise justification, nor information derived from those justifications or offers...". As with the broader records destruction provisions discussed above, this prohibition amounts to CMS putting its thumb on the scale of transparency as the only entity involved in the negotiation program who can control and confirm information flows. This one-sided information control heightens the ultimate public complaint that the entirety of the "negotiation" process is anything but. Rather, optically – and in practice – it appears CMS is proposing to control the entirety of the negotiation process, and to stifle any outside public discussion of the negotiation process itself. BIO disagrees with this approach and recommends CMS abandon it.

Further, the blanket "gag" sought in the proposed guidance raises several practical and Constitutional concerns. From a broader regulatory standpoint, certain regulatory agencies (*e.g.* The Securities and Exchange Commission) might well have conflicting standards for materiality determinations in disclosures made by publicly traded companies. We would argue that the exclusion in the guidance

¹³⁵ *Evans v. Wilkerson*, 605 F.2d 369, 371 (7th Cir. 1979).



from the disclosure prohibition based on state and federal law might not go far enough in covering certain regulatory obligations – both at the federal and state level. Particularly when considered in context with the records destruction obligations imbued in the guidance as well.

What is more, CMS appears to be making a more general affront to the protected speech of affected manufacturers. As has been reaffirmed many times before, prior restraints on speech are presumptively unconstitutional.¹³⁶ The government faces a heavy burden in showing a compelling interest in keeping negotiation discussions private, and we fail to see a legitimate reason why the government's interests are so advanced by muzzling private companies in the context of Medicare price negotiation discussions.¹³⁷ In fact, in this instance, any potential disclosure by a manufacturer would likely relate to truthful information that is, at a minimum, of significance to at least a portion of the public involved in the transaction of health insurance and health consumption. As such, we recommend CMS abandon these burdensome and unnecessary confidentiality and anti-disclosure provisions.

D. Special considerations in setting the MFP

It is vital that, in setting the MFP, CMS impose on itself bright-line limitations that mitigate the negative effects of the IRA and the MFP on patient access and on therapeutic innovation. BIO strongly urges CMS to adopt the following limitations.

BIO asks CMS to commit to a policy where it will not set the MFP below a price shown to imperil patient access (or otherwise below the MFP ceiling).

It is basic economics that centralized price-setting risks curtailing access to the supply of medicines.¹³⁸ If the government mandates a price too far below the price that would have been set by the free market, there will be an inevitable and profound mismatch between demand and supply.¹³⁹

BIO urges CMS, in carrying out the Negotiation Program, to be attuned to the risk to patient access if the MFP is set unduly low. The stakes are too high for CMS not to give due weight to such risk. The implication of a supply-demand mismatch is not limited to some economist's spreadsheet. Rather, it

¹³⁶ See, e.g., *Near v. Minnesota* 283 U.S. 697 (1931).

¹³⁷ As has been reaffirmed in many instances by the US Supreme Court, the government must articulate a compelling government need for the negotiation to remain out of the public discourse and must simultaneously introduce a narrowly tailored method for so restricting this discussion. In the context of this guidance, we see no such articulation of either a compelling need nor a narrow restriction. In fact, we see just the opposite. See, e.g., *New York Times Co. v. United States*, 403 U.S. 713 (1971).

¹³⁸ S. Atlas, *How to Reduce Prescription Drug Prices: First, Do No Harm*, 117 *Modern Med.* 14, 14 (2020).

¹³⁹ Rent control is the classic Economics 101 illustration: Price controls on rental stock result in undersupply; the result is a net societal loss of utility relative to the pareto optimal price. See, e.g., E. Glaser & E. Luttmer, *The Misallocation of Housing Under Rent Control*, 93 *Am. Econ. Rev.* 1027, 1027 (2003).



could mean the difference between millions of patients having access to life-saving medicines and empty shelves at the pharmacy counter. Indeed, the House Committee on Ways and Means has estimated that loss of innovation due to price controls could result in as many as “42 million patients without the medicine they need.”¹⁴⁰

The risk to longer-term innovation and development of new medicines is even more profound. One recent study by the University of Chicago concluded that the “mid-range effect” of price controls is 254 fewer new drug approvals; the researchers conservatively estimated that the loss in life from the price controls accordingly is twenty times larger than our country’s losses from the COVID-19 pandemic.¹⁴¹ Another study of the European experience found that a “10% drop in the price of medicines in price-controlled [European Union] markets was associated with . . . an 8% increase in the delay of access to medicines.”¹⁴² Still other studies have demonstrated that government price-setting is associated with dramatic declines in early research, which, of course, is the fundamental precursor to a robust and growing pipeline of new therapies targeting areas of unmet medical need.¹⁴³

Therefore, CMS should commit to a policy under which it will not set the MFP below a price shown to further imperil patient access (or otherwise below the MFP ceiling). This approach would help strike an equitable balance, giving weight to the objective of reducing prices today while also mitigating the risk that price controls will significantly imperil the drug supply or further curtail the development of the transformative medicines of tomorrow.

BIO also asks CMS to commit to setting the MFP at the MFP ceiling where failing to do so would further curtail therapeutic innovation.

It is vital that the Negotiation Program strike an appropriate balance such that blunt reductions in Medicare expenditures do not come at the expense of ongoing innovation that yields new and potentially life-saving medicines. Accordingly, BIO urges CMS to commit to setting the MFP at the MFP ceiling where doing otherwise would imperil therapeutic innovation, including in the following circumstances (not exhaustive):

¹⁴⁰ U.S. House Comm. on Ways & Means, Analysis: Americans Don’t Support Surrendering Innovation, <https://waysandmeans.house.gov/analysis-americans-dont-support-surrendering-innovation-for-democrats-drug-price-controls/> (Aug. 4, 2022).

¹⁴¹ See T. Phillipson & T. Durie, The Evidence Base on the Impact of Price Controls on Medical Innovation 1 (2021) (loss in life estimate was over a ten-year time period), available at https://bfi.uchicago.edu/wp-content/uploads/2021/09/BFI_WP_2021-108.pdf.

¹⁴² D. Schulthess & H. Bowen, *The Historical Impact of Price Controls on the Biopharma Industry*, Vital Transformations (Nov. 22, 2021).

¹⁴³ See T. Abbott & J. Vernon, *The Cost of US Pharmaceutical Price Reductions: A Financial Simulation Model of R&D Decisions*, 28 Managerial & Decision Econ. 293 (2007).



First, for a drug (small molecule), the MFP should not be set below the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.

To be selected for negotiation, biologics (large molecules) must be at least eleven years post-licensure, while drugs (small molecules) must be at least seven years post-approval.¹⁴⁴ On account of the approximately two-year time lag between selection for negotiation and application of the MFP, an MFP cannot apply to a biologic until at least approximately thirteen years post-licensure; in contrast, an MFP cannot apply to a drug until at least approximately nine years post-approval. To help preserve small molecule innovation in parity with large molecule innovation, we ask that, for a small molecule, CMS set the MFP at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.

Studies show that most products (whether small or large molecules) achieve modest levels of annual sales in their first five years on the market.¹⁴⁵ Thus, manufacturers may seek the economic benefit of an additional four-year shelter from selection for negotiation by focusing research and development on biologics instead of drugs.

Thus, we ask that CMS act to better balance the incentives regarding small molecule drug and biologic development by setting the MFP for a small molecule drug at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.

Second, the MFP should not be set below the MFP ceiling during any year of the price applicability period into which patent protection extends.

CMS must consider a number of factors in determining the MFP for a selected drug, including “[d]ata on pending and approved patent applications.”¹⁴⁶ We ask CMS to ascertain whether, based on information submitted by the manufacturer, the selected drug will have any remaining patent protection at the start of the price applicability period and, if so, set the MFP at the MFP ceiling price for any year during such period into which such patent protection extends.

¹⁴⁴ SSA § 1192(e)(1).

¹⁴⁵ QuintilesIMS Inst., *Lifetime Trends in Biopharmaceutical Innovation: Recent Evidence and Implications*, at 2 (Jan. 2017).

¹⁴⁶ SSA § 1194(e)(1)(D).



The statute permits a drug to be subject to an MFP nine years post-approval and a biologic to be subject to an MFP thirteen years post-licensure.¹⁴⁷ By the time the price applicability period for a selected drug begins, the product’s regulatory exclusivity period likely will have expired—but not necessarily its patent protection period.¹⁴⁸ In other words, given that a patent protection period can extend beyond a regulatory exclusivity period, it may very well be the case that there will be remaining patent protection for a selected drug that extends into the price applicability period.

In the Initial Guidance, CMS proposes that, if a selected drug “has patents and exclusivities that will last a number of years,” CMS may adjust the “preliminary price” downward.¹⁴⁹ This is the opposite of what the policy should be. A selected drug’s ongoing patent protection supports a higher “preliminary price”—and, indeed, an MFP equal to the MFP ceiling. This is key to supporting pharmaceutical and biotechnology innovation in developing drugs and biologics that treat serious diseases.

It is a long and expensive process to bring a chemical or biological product from research and development to market, and many candidates do not make it through the process. To encourage innovation by rewarding manufacturers for their research and development investments and efforts, the federal government awards pharmaceutical and biotechnology companies with patent protection for a specified period of time. The patent protection period affords a manufacturer the opportunity to recover its research and development costs—not only for the drug for which the patent was awarded but also for other research and development investments that the manufacturer made. To support continued innovation, CMS should honor any remaining patent protection for a selected drug by specifying that the MFP will be set at the MFP ceiling during any year of the price applicability period into which such patent protection extends.

Third, the MFP should be set at the MFP ceiling until at least the first year during the price applicability period that starts after the date on which the most recently approved indication is thirteen years post-approval.

Innovation should not end with the approval of a first indication. Rather, finding novel uses for existing therapies is “essential for maximizing medicines’ therapeutic utility.”¹⁵⁰ Developers of

¹⁴⁷ *Id.* § 1192(e)(1).

¹⁴⁸ See FDA, Frequently Asked Questions on Patents and Exclusivity, available [here](#) (last accessed Mar. 2023).

¹⁴⁹ Initial Guidance at 53.

¹⁵⁰ B. Sahragardjoonegani et al., Repurposing existing drugs for new uses: A cohort study of the frequency of FDA-granted new indication exclusivities since 1997, 14 J. of Pharmaceutical Policy & Practice 1 (2021).



drugs and biologics therefore devote countless hours and untold capital to research and development of new indications, thereby expanding treatments to additional disease states and patient populations.¹⁵¹

In recent years, new indications have spurred vital medical breakthroughs across countless critical medical conditions. For example, new indications have been vital “to increase the portfolio of available effective cancer chemotherapeutic agents for patients.”¹⁵² Similarly, the repurposing of existing therapies has played a critical role in meeting the otherwise unmet needs of patients with rare medical conditions.¹⁵³

The seven- and eleven-year selection clocks work to extinguish such innovation by actively disincentivizing a manufacturer from making the considerable investment necessary to obtain approval of a new indication, given that such indication would run on the same selection clock. CMS must act to mitigate this concern by committing to setting the MFP at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the most recently approved indication is thirteen years post-approval. Such limitation on the setting of the MFP would provide greater certainty to manufacturers as they consider ongoing investment in research and development of new indications. This could avoid wholesale extinguishment of therapeutic innovation, to the detriment of patients with serious unmet medical needs, on account of the seven- and eleven-year selection clocks.

Fourth, the MFP should not be set below the MFP ceiling for vaccines recommended by the Advisory Committee on Immunization Practices (ACIP) at the Centers for Disease Control (CDC). Vaccination is often cited among the 10 greatest public health achievements of the century. In addition to their societal benefit, vaccines deliver significant benefit to individuals throughout their lifetime and allow older individuals to remain healthier and productive in their later years of life. The importance of vaccines was recognized in the IRA, which eliminated cost sharing for vaccines in Medicare Part D, building on the precedent in Medicare Part B where there was no cost sharing for vaccines. Because of the high value that vaccines confer not only to Medicare beneficiaries but to society as a whole, the MFP for vaccines recommended by the ACIP should not be set below the MPF ceiling.

¹⁵¹ See *id.* at 1–2 (noting the significant time and cost associated with obtaining approval of a new indication).

¹⁵² S. Islam, et al., Repurposing existing therapeutics, its importance in oncology drug development: Kinases as a potential target, 88 Br. J. Clin. Pharmacol. 64 (2021).

¹⁵³ See P. Ayyar et al., Repurposing – second life for drugs, 69 Pharmacia 51, 52 (2022).



IV. Negotiation Factors

For purposes of negotiation of the MFP, the statute (SSA 1194 (e)) directs CMS to consider the following factors:

- Manufacturer-specific data (SSA 1194 (e)(1)): Research and development costs and the extent to which the manufacturer has recouped such costs; current unit costs of production and distribution; prior federal financial support for discovery and development; and data on pending and approved patents and exclusivity; and market data and revenue and sales volume data.
- Evidence about alternative treatments (SSA 1194 (e)(2)): the extent to which the drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such alternative; FDA-approved prescribing information for the drug and the alternatives; comparative effectiveness of the drug and the alternatives, including effects on specific patient populations; the extent to which the drug and the alternatives address unmet medical need.

The statute also directs CMS not to use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

A. **Evidence on therapeutic alternatives and unmet need**

CMS should emphasize factors related to clinical value and unmet need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.

In developing a starting point for the initial offer, CMS proposes to utilize the net price for identified therapeutic alternatives and then adjust this starting point based on the review of the clinical evidence to develop a “preliminary price.” CMS will then consider the manufacturer specific data under section 1194(e)(2) and may adjust the preliminary price upward or downward. When there is no therapeutic alternative CMS would adjust the starting point based on how the selected drug fills an unmet medical need.

The proposed approach outlined by CMS is vague, and CMS’s intent is unclear. We strongly support an approach that emphasizes factors related to clinical benefit and unmet medical need and de-emphasizes manufacturer specific data elements such as cost of production and research and development costs – CMS should clarify how it will weight these factors in that regard. CMS should consider and prioritize high quality, robust real-world evidence (RWE), evidence provided by clinicians with the necessary expertise, as well as evidence submitted by manufacturers – who have a vast depth and breadth of



clinical and scientific expertise regarding their marketed therapies. CMS should also focus on patient-centered outcomes and the broader societal benefit conferred by a therapy. Further, providing higher relative MFPs to products that have advanced patient care and address unmet medical need will help maintain investment in assets and clinical programs that show scientific promise. At the same time, it is critical that CMS is transparent in its approach in determining therapeutic alternatives to selected drugs and provides a strong justification that the identified therapeutic alternatives are appropriate and are primarily driven by clinical guidelines and patient need versus cost.

It is essential that CMS clarify how it will evaluate the evidence it receives from different stakeholders and how such evidence will be considered in identifying therapeutic alternatives and setting the MFP.

CMS says it would adjust the preliminary price based on the totality of the relevant information and evidence submitted and gathered through the agency's analysis based on the clinical benefit the selected drug provides compared to its identified therapeutic alternatives. We support an approach that considers a wide range of high quality, robust evidence, including RWE. Further, information submitted by manufacturers should be considered a high priority in CMS's review as manufacturers have deep and unique expertise in their therapeutic areas of focus.

CMS should be transparent and provide sufficient detail regarding its framework for how different evidence was used to inform the identification of therapeutic alternatives for a selected drug, as well as the establishment of the preliminary price as well as the initial offer and response to any counteroffer, including what evidence was most impactful in CMS' analysis and why. CMS' review of the evidence should be patient-centered and have a focus on health equity and reducing disparities. To that end, we strongly support CMS's confirmation that evidence that uses discriminatory approaches such as QALYs will not be considered. We also note that other measures that have been often promoted as alternatives to QALYs – such as the Equal Value of Life Years Gained (evLYG) – are also problematic as they limit the value of interventions that both extend life and improve the quality of life – and CMS should similarly reject them. In reviewing the evidence CMS should recognize both the current and future value of therapies and remain flexible to keep pace with innovations in science and technology. Further, evidence on a therapy should be viewed in the context of its benefits to the Medicare program, as well as the overall health care system.

We recommend that CMS provide manufacturers with robust detail regarding its analysis of evidence throughout the negotiation process and provide manufacturers with opportunities for discussion and dialogue, including before CMS's initial offer in February 2024 and in its identification of therapeutic alternatives that will be used in setting the MFO. CMS should also provide a line of sight into its assessment of the evidence for the broader stakeholder community, so as to ensure appropriate



transparency and accountability not just to manufacturers but to Medicare beneficiaries and to providers and other key stakeholders.

We are concerned that CMS’s proposed definition of unmet medical need is too limiting; the agency should use a more robust definition. We recommend that CMS look to the FDA’s definition outlined in its “Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics.”¹⁵⁴ Under the FDA guidance, “An unmet medical need is a condition whose treatment or diagnosis is not addressed adequately by available therapy. An unmet medical need includes an immediate need for a defined population (i.e., to treat a serious condition with no or limited treatment) or a longer-term need for society (e.g., to address the development of resistance to antibacterial drugs).”

B. Submission of Information on Negotiation Factors Related to Therapeutic Alternatives and Unmet Need (Section 1194(e)(2))

CMS’s approach and processes for collecting information on the negotiation factors related to therapeutic alternatives and unmet medical need should ensure that a robust, comprehensive set of information submitted by manufacturers– with any necessary supplemental material – will be accepted and considered by CMS.

The negotiation guidance references the Negotiation Data Elements ICR, which describes how CMS intends to collect data on the negotiation factors. We are concerned that CMS’s approach may be too limiting in practice and will not allow for a robust submission of information - including any supplementary material – by manufacturers. We will be providing more detailed comments on the ICR, but note Questions 40 through 43, which collect information on prescribing data, therapeutic impact and comparative effectiveness, comparative effectiveness in specific populations, and unmet medical needs. The data fields are limited to 1,000-3,000 words, which is insufficient in length. Further, the data fields do not seem to contemplate submission of complementary information, such as charts and tables. We strongly recommend that CMS reconsider its approach and permit manufacturers to submit any information they determine relevant to the negotiation process (including information not related to the negotiation factors enumerated in the statute). Further, CMS should be required to consider all such information, not just the negotiation factors in sections 1194(e)(1) and 1194(e)(2).

¹⁵⁴ <https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf>



C. Submission of Manufacturer-Specific Data (Section 1194(e)(1))

We understand that the IRA requires CMS to consider factors under both section 1194(e)(1) and section 1194(e)(2). **However, as noted above, we believe CMS should de-emphasize factors the manufacturer-specific data in section 1194(e)(1) and focus on the factors that matter most to patients – those that are focused on clinical value and unmet need. In addition, to address issues that we highlight below, we recommend that, in lieu of the proposed standardized definitions, CMS allow manufacturers to use reasonable assumptions (with accompanying justifications) regarding the information they submit on the manufacturer-specific data.**

There are important considerations that will make it difficult – if not impossible – for CMS to standardize the definitions for the manufacturer-specific factors. For example, regarding research and development costs, a key issue for CMS to consider is that companies, and investors, invest in research and development for “programs” in a specific disease area, not simply discrete drugs. A program can have many drugs or biologicals at different stages of development each with multiple indications, and all which would factor into the research and development costs for an FDA-approved or licensed therapy. This can include thousands and sometimes millions of compounds that could be screened early in the research and development process, with a success rate of less than 12%.¹⁵⁵

Further, it can be misleading to approximate “value” using research and development costs. Not all companies conduct research and development in the same manner. Some smaller companies might undertake single-therapeutic, high-risk approaches to developing a compound, while many others, often bigger companies, conduct research using the “programs,” as noted. These differences in the way research and development can be conducted could disadvantage companies in negotiation if manufacturer-specific data is too heavily relied upon for “value.”

Looking at research and development costs in the post-market setting can also be misleading because of ongoing costs that are difficult to quantify. For example, the FDA requires post-market safety monitoring, these costs can also be augmented if a manufacturer must utilize FDA-mandated risk evaluation and mitigation strategies (REMS), something to which not every manufacturer is subjected. Another example is costly post-market clinical trials that can take years.

We also are concerned with CMS’s proposed requirement to collect information that is not collected today – once example is net revenue “without patient assistance programs.” It is unclear why CMS would be collecting data in this manner and the underlying implication of patient assistance programs on price.

¹⁵⁵ Biopharmaceutical Research and Development: The Process Behind the Medicines, PhRMA. 2015. Accessed: 03/28/2023. http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf



In other areas, the definitions CMS proposes are unclear, which will make it difficult for manufacturers to comply with submission requirements. For example, regarding data on approved and pending patents, clarifications are required to better define the patents and pending patent applications that must be disclosed. More precision is required where CMS is asking for patents “relating” or “linked to” the selected drug, as it is unclear what CMS means – related or linked how? In this respect, we also note that “patent” and “patent application” are well-understood terms of art that don’t require further definition in the CMS guidance. For example, the CMS guidance definition of a “pending patent application” specifies any patent application “for which a patent number has not been issued.” This definition would plainly include applications that are not, in fact, pending because they have been abandoned. An “approved patent application” presumably means a patent application that has received a notice of allowance, meaning that it is still a pending patent application (and not a “patent”) that does not require a special definition. And a “patent” comes into existence not on the date a patent application is “approved,” but on the date a patent is issued, and the official patent grant is transmitted. We recommend deleting the special definitions of “pending patent application,” “approved patent application,” and “expired patent,” and to change the operative language as suggested in our proposed edits below.¹⁵⁶

Patents, Exclusivities, and Approvals

For the purposes of describing patents, exclusivities, and approvals to be collected for use in the Negotiation Program for the selected drug, as described in section 1194€(1) of the Act and section 50.1 of this memorandum, CMS intends to adopt the definitions described in this subsection.

- *CMS considers patents relevant to this data to include:*
 - *all patent applications pending in the USPTO, international patent applications filed under the Patent Cooperation Treaty that designate the United States, and all U.S. patents, that are owned by, licensed to, or controlled ~~pending and approved patent applications, including expired and non-expired approved patents, submitted, sponsored, licensed, and/or acquired by the Primary Manufacturer relating to the,~~ and that claim the selected drug, a constituent part of the selected drug, or an approved method of using the selected drug as of September 1, 2023;*
 - *U.S. patents ~~linked to~~ that claim the selected drug, a constituent part of the selected drug, or an approved method of using the selected drug where the Primary Manufacturer is not listed as the assignee/applicant but with respect to which the manufacturer has enforcement rights (for example, for a joint venture product); and any patent that is with respect to the selected drug included in a list published under*

¹⁵⁶ Note that the nomenclature of “Primary Manufacturer” is retained in the edits we suggest but we note our comments later in this section that raise concerns with the “Primary Manufacturer” and “Secondary Manufacturer” construct.



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section 351(k)(9) of the Public Health Service Act or section §505(j)(7) of the Federal Food, Drug, and Cosmetic Act, ~~patent applications, pending and approved,~~ for which a claim of patent infringement could reasonably be, or has been, asserted against a person engaged in the unlicensed manufacture, use, or sale of the selected drug ~~in any form.~~

More fundamentally, CMS states it will consider the length of available patents and exclusivities and, if such patents and exclusivities will last for a number of years, the Agency may consider reducing the preliminary price downward. BIO strongly opposes such an approach. Rather, remaining patents and exclusivities should only be used to justify an *increase* in the preliminary price.

Regarding data on prior federal financial support in discovery and development, important contextual information should be considered by CMS. The biopharmaceutical industry's role in the U.S. research ecosystem is to undertake the clinical research and development required to advance basic science research by entities such as the National Institutes of Health (NIH) into safe and effective treatments available to patients. In 2018, the biopharmaceutical industry invested \$102 billion in R&D, most of which was focused on clinical research. Meanwhile, the entire NIH budget in 2018 was \$35.4 billion, only 8% of which was focused directly on clinical research.

Of note, of the 23,230 NIH grants in the year 2000 that were linked by NIH supported patents to 41 investigational drugs, only 18 had gained FDA approval by 2020. In fact, total private investment for these 18 approved medicines exceeded NIH funding by substantial orders of magnitude: \$44.2 billion in private investment compared to \$670 million in NIH. These findings are consistent with scholarship describing the complementary roles of public and private R&D funding, and the significant long-term investments shouldered by industry with no guarantee of approval. In fact, just 7.9% of medicines in clinical development are ultimately approved by the FDA.¹⁵⁷

We also note our concern with the proposal to hold a Primary Manufacturer responsible for submitting applicable information concerning a Secondary Manufacturer. A Primary Manufacturer has no inherent legal authority to compel a Secondary Manufacturer to act or not act, including to share such information. It would be fundamentally unfair and legally problematic for CMS to threaten a Primary Manufacturer with significant civil monetary penalties (CMPs) for failure to do the impossible. We note that this same concern pervades the Initial Guidance, given the numerous contexts in which CMS proposes to hold a Primary Manufacturer responsible for the action or inaction of a Secondary Manufacturer.

¹⁵⁷ Clinical Development Success Rates and Contributing Factors 2011-2020. Available at [bio.org](https://www.bio.org).



V. MFP Ceiling

A. Background

The calculation of the MFP ceiling, which represents the maximum possible MFP, is the lowest of three amounts:

- (1) the “applicable percent” of the Average Non-FAMP for 2021 (or, if there is such Non-FAMP, the Average Non-FAMP for the first full year following market entry), as increased by a Consumer Price Index for All Urban Consumers (CPI-U) factor;¹⁵⁸
- (2) the “applicable percent” of the Average Non-FAMP for the year before the year of the selected drug publication date (except for IPAY 2026);¹⁵⁹ or
- (3) (a) for a Part D drug, the sum of each “plan specific enrollment weighted amount” for each prescription drug plan (PDP) or Medicare Advantage prescription drug (MA-PD) plan;¹⁶⁰ or
(b) for a Part B drug, the Part B payment amount for the year before the year of the selected drug publication date.¹⁶¹

The “applicable percent” is 75 percent for “short-monopoly drugs,”¹⁶² 65 percent for “extended-monopoly drugs,”¹⁶³ and forty percent for “long-monopoly drugs.”¹⁶⁴

B. Average Non-FAMP

BIO recommends that, in defining Average Non-FAMP, CMS abandon its proposal to create a new price point calculated based on the four quarters of a calendar year, and instead simply adopt the existing annual Non-FAMP, calculated based on the four quarters of a federal fiscal year, under the Veterans Health Care Act of 1992 (VHCA).

As set forth above, Average Non-FAMP is calculated as part of determining the MFP ceiling.¹⁶⁵ Average Non-FAMP is a statutory term of art meaning “the average of the non-Federal average manufacturer

¹⁵⁸ SSA § 1194(c)(1)(A), (C). The CPI-U adjustment applies from September 2021 (or December of the first full year following market entry) to September of the year before the year of the selected drug publication date.

¹⁵⁹ *Id.*

¹⁶⁰ *Id.* § 1194(c)(1)(A), (B)(i), (2).

¹⁶¹ *Id.* § 1194(c)(1)(A), (B)(ii).

¹⁶² *Id.* § 1194(c)(3)(A) (defining “short monopoly drug” as a selected drug that is not an “extended-monopoly drug” or “long-monopoly drug”).

¹⁶³ *Id.* § 1194(c)(3)(B); *see also id.* § 1194(c)(4) (defining “extended monopoly-drug”).

¹⁶⁴ *Id.* § 1194(c)(3)(C); *see also id.* § 1194(c)(5) (defining “long-monopoly drug”).

¹⁶⁵ *Id.* § 1194(c)(1)(A), (C).



price (as defined in section 8126(h)(5) of title 38, United States Code) for the 4 calendar quarters of the year involved.”¹⁶⁶

The statute does not specify which four quarters are “the 4 calendar quarters of the year involved but notably cross-references 38 U.S.C. § 8126(h)(5), i.e., the VHCA. As such, the statute effectively instructs CMS to calculate Average Non-FAMP by reference to how annual Non-FAMP is calculated under the VHCA.

The VHCA requires manufacturers to calculate and report quarterly Non-FAMPs and an annual Non-FAMP—but does not require manufacturers to calculate and report an “average” Non-FAMP based on the four quarters of a calendar year. Rather, the annual Non-FAMP is calculated based on the four quarters of a federal fiscal year—which runs from October 1 through September 30.¹⁶⁷

As such, the annual Non-FAMP is a stand-alone weighted average calculation based on data from the fourth quarter of a calendar year through the third quarter of the subsequent calendar year (i.e., the four quarters of a federal fiscal year).¹⁶⁸ The most coherent policy would be for CMS to adopt the same approach to calculating Average Non-FAMP for a year under the Negotiation Program. Given that the statute expressly cross-references the VHCA in the course of defining Average Non-FAMP, there is every reason to think that Congress wanted CMS to maximize alignment as between Average Non-FAMP and the annual Non-FAMP under the VHCA, rather than creating an entirely new price point.

In the Initial Guidance, however, CMS does not propose to borrow the established VHCA framework. Rather, CMS proposes to calculate Average Non-FAMP by reference to the four quarter of a calendar year.¹⁶⁹ This approach is inefficient and unnecessarily burdensome for both CMS and manufacturers. Under the proposal, the Agency will be obligated to develop, implement, and oversee a completely new process to facilitate collection of new pricing data, as the Agency cannot benefit from the efficiencies of the well-established process that VA has already put into place—because the VHCA approach is, as noted above, tied to a federal fiscal year, rather than a calendar year. By contrast, if the Agency instead were to borrow the existing VHCA framework, Average Non-FAMP would be equated with a price point that already exists, and all stakeholders would benefit from the resulting efficiencies.

¹⁶⁶ *Id.* § 1194(c)(6).

¹⁶⁷ For example, the data used to calculate the annual Non-FAMP for 2021 cover the period from October 1, 2020, through September 30, 2021.

¹⁶⁸ The annual and quarter 3 Non-FAMPs submitted to the Department of Veterans Affairs (VA) are used to calculate the Federal Ceiling Price (FCP), which caps pricing under VA Federal Supply Schedule contracts. Manufacturers are required to submit quarters 1, 3, and 4 Non-FAMPs, too, but these price points have no impact on the price paid by the federal government. While the data used to calculate these quarterly Non-FAMPs are incorporated into the four quarters of data used to calculate the annual Non-FAMP, these quarterly Non-FAMPs themselves are not used to calculate the annual Non-FAMP.

¹⁶⁹ Initial Guidance at 42–44.



If CMS does not reverse course, BIO agrees that CMS’s framework should be based on a weighted average.¹⁷⁰

A weighted average is consistent with the VHCA framework expressly cross-referenced in the statutory definition of Average Non-FAMP. A such, a weighted average better aligns to Congress’s intent.

More importantly, use of a weighted average will objectively enhance accuracy because it will account for differences in volume across quarters and therefore create the most accurate picture of average wholesaler pricing. Such enhanced accuracy is why Congress has consistently required the use of weighted averages across the various federal pricing programs associated with federal health care programs: VHCA (Non-FAMP), Medicaid (AMP), and Medicare (ASP) all use weighted averages, not simple averages.

Congress has consistently required the use of weighted averages because simple averages are less accurate. Simple averages result in over-valuation of sales in quarters with lower sales volumes, and under-valuation of sales in quarters with higher sales volumes. As such, it is critically important that CMS use a weighted average to ensure more accurate calculations of Average Non-FAMP, and we concur with CMS’s proposal to do so.

The Agency should establish an exceptions process to account for restatements and anomalies.

An exceptions process is vital. There will inevitably be situations where Average Non-FAMP will need to be restated in light of data errors or other issues identified after the fact or where an unusual circumstance will result in an anomalous Average Non-FAMP.

- **Non-FAMP restatements.** CMS must consider how it will address situations in which a Non-FAMP that is used for an MFP calculation is restated by the manufacturer and approved by VA. VA has long recognized the need for manufacturers to be able to restate a Non-FAMP where the reported Non-FAMP is determined to be inaccurate (e.g., sales data flaws, data system problems). The VA experience has demonstrated that restatements are not uncommon, with adjustments of contract pricing facilitated based on restated Non-FAMPs and FCPs. The Agency must expressly account for the need for such restatements—but the Initial Guidance does not do so.

¹⁷⁰ *Id.* at 43.



- **Non-FAMP anomalies.** The VA’s experience reveals a variety of circumstances where an anomalous Non-FAMP can arise due to a misalignment of sales dollars and units. This can occur due to lagged sales, market shortages, or various other factors. VA has developed various exceptions and workarounds for calculating FCPs when there are Non-FAMP anomalies. It is vital that CMS develop its own processes for addressing anomalous Average Non-FAMPs. Any approach adopted by CMS needs to be flexible to account for the wide range of circumstances that can result in an anomalous Average Non-FAMP.¹⁷¹ But the Initial Guidance is silent on any such flexibilities.

BIO encourages CMS to adopt an exceptions process to account for Average Non-FAMP restatements and anomalies. In doing so, CMS should clarify how such process affects the MFP ceiling and, ultimately, the MFP.

C. Extended- and long-monopoly drugs

CMS should clarify whether the time period for determining whether a selected drug is an extended- or long-monopoly drug runs to the start of the applicable IPAY, or to the applicable selected drug publication date.

As set forth above, there are three options for setting the MFP ceiling. Two of these options look to the “applicable percent” of the applicable Average Non-FAMP.¹⁷² By statute, the “applicable percent” varies based on whether the drug is a short-, extended-, or long-monopoly drug.¹⁷³

With limited exceptions, extended monopoly drugs are, “with respect to an initial price applicability year, selected drug[s] for which at least 12 years, but fewer than 16 years, have elapsed since the date of approval . . . or . . . licensure,”¹⁷⁴ and long-monopoly drug are, “with respect to an initial price applicability year, selected drug[s] for which at least 16 years have elapsed since the date of approval . . . or licensure.”¹⁷⁵ Short-monopoly drugs are all other selected drugs.¹⁷⁶

Notably, the statute is silent as to the date to which the twelve- or sixteen-period that defines an extended- or long-monopoly drug runs. In the Initial Guidance, CMS takes inconsistent positions. On the one hand, CMS states that, for IPAY 2026, a delay request may be submitted where a reference

¹⁷¹ For example, in certain cases, it may be prudent for CMS to account for an Average Non-FAMP anomaly by looking to the prior year’s figures; in other cases (e.g., a new product), this may not be possible.

¹⁷² SSA § 1194(c)(1).

¹⁷³ *Id.* § 1194(c)(3).

¹⁷⁴ *Id.* § 1194(c)(4)(A).

¹⁷⁵ *Id.* § 1194(c)(5)(A).

¹⁷⁶ *Id.* § 1194(c)(3)(A).



biologic will have been “licensed for between 12 and 16 years prior to the start of the initial price applicability year on January 1, 2026.”¹⁷⁷ On the other hand, in “Figure 2: Monopoly Types and Applicable Percentage for Initial Price Applicability Year 2026,” CMS conveys that, for IPAY 2026, it will count the 16-year period that defines a long-monopoly drug to September 1, 2023, i.e., the selected drug publication date for IPAY 2026.¹⁷⁸ In other words, CMS is inconsistent as to whether the twelve- or sixteen-year period that defines an extended- or long-monopoly drug runs to the start of the applicable IPAY, or to the applicable selected drug publication date.

BIO asks CMS to clarify its intended interpretation in light of the conflicting language in the Initial Guidance.

D. MFP ceiling for Part D drugs

BIO disagrees with CMS’s intended approach for calculating the MFP ceiling option specific to Part D drugs. CMS must calculate the MFP ceiling under such option exclusive of manufacturer price concessions unless they are passed through at the point of sale, consistent with CMS’s long-standing policy governing the Part D negotiated price.

As set forth above, one of the three options for determining the MFP ceiling with respect to a Part D drug is the sum of each “plan specific enrollment weighted amount” for each PDP or MA-PD plan.¹⁷⁹ Congress specified that the “plan specific enrollment weighted amount” is determined by reference to the Part D negotiated price.¹⁸⁰ As such, Congress made clear that the “plan specified enrollment weighted amount” is to be determined by reference to CMS’s policies governing the Part D negotiated price.

This is not what CMS proposes. In the Part D context, CMS has long defined the Part D negotiated price to be “inclusive of all price concessions from network pharmacies, except those contingent price concessions that cannot reasonably be determined at the point-of-sale”—but not to require inclusion of price concessions from manufacturers.¹⁸¹ Rather, PDPs and MA-PDs may choose to include manufacturer price concessions in the Part D negotiated price to the extent that they are passed through at the point of sale: “Part D sponsors are allowed, but generally not required, to apply rebates

¹⁷⁷ Initial Guidance at 17 (emphasis added).

¹⁷⁸ See Initial Guidance at 45.

¹⁷⁹ SSA § 1194(c)(1) (A), (B)(i).

¹⁸⁰ *Id.* § 1194(c)(2).

¹⁸¹ 42 C.F.R. § 423.100 (emphasis added). CMS has issued a rule that will revise the Part D negotiated price definition effective January 1, 2024. But such revision does not alter the fact that the Part D negotiated price does not require inclusion of manufacturer price. See 87 Fed. Reg. 27,704, 27,899 (May 9, 2022).



and other price concessions at the point of sale to lower the price upon which beneficiary cost-sharing is calculated.”¹⁸²

CMS’s Initial Guidance ignores this long-standing policy defining the Part D negotiated price. For purposes of calculating the MFP ceiling under the option specific Part D drugs, CMS instead proposes to use Direct and Indirect Remuneration (DIR) data—rather than solely PDE data—to calculate the “plan specific enrollment weighted amount.”¹⁸³ Notably, unlike PDE data, DIR data reflect all price concessions, including those received from manufacturers that are not passed through at the point of sale.¹⁸⁴

CMS’s proposed approach is contrary to statute, which makes clear that the MFP ceiling option must be determined by reference to the Part D negotiated price. By choosing expressly to define the MFP ceiling option by reference to the Part D negotiated price, Congress required such option to be calculated in accordance with policy governing the calculation of the Part D negotiated price. Any contrary approach would render meaningless Congress’s express choice to use the Part D negotiated price as the statutory reference point.

In addition to being inconsistent with statutory text and Congressional intent, CMS’s proposal also would create significant unnecessary complexities. It would be more burdensome for the Agency to determine the MFP ceiling for Part D drugs if the Agency were to apply a standard that is inconsistent with the Part D standard. In addition, it would impose a new and unfamiliar approach on pharmacies, plans, pharmacy benefit managers (PBMs), manufacturers, and other stakeholders, and would thereby increase the risk of confusion or error that could result in an erroneous MFP.

BIO urges CMS to abandon this proposal and instead align the Part D drug-specific MFP ceiling option with CMS’s long-standing policy defining the Part D negotiated price, consistent with the requirements of the statute.

VI. Providing Access to the MFP

A. Background

Under the Negotiation Program, the manufacturer of a selected drug must provide access to the MFP to:

¹⁸² 87 Fed. Reg. at 27,835 (the Part D negotiated price is “the price paid to the network pharmacy or other network dispensing provider for a covered Part D drug dispensed to a plan enrollee that is reported to CMS at the point of sale by the Part D sponsor”).

¹⁸³ Initial Guidance at 40.

¹⁸⁴ CMS, Medicare Part D – Direct and Indirect Remuneration (DIR) (Jan. 19, 2017).



- With respect to a Part B drug, “hospitals, physicians, and other providers of services and suppliers with respect to [individuals who are enrolled under Part B, including individuals who are enrolled in an Medicare Advantage (MA) plan, if payment may be made under Part B for the drug, and who are furnished the drug];”¹⁸⁵ and
- With respect to a Part D drug, “[individuals who are enrolled in a PDP or MA–PD plan if the drug is covered under such plan, and who are dispensed the drug,] at the pharmacy, mail order service, or other dispenser at the point-of-sale of such drug (and . . . to the pharmacy, mail order service, or other dispenser, with respect to such . . . individuals who are dispensed such drugs).”¹⁸⁶

MFP-340B duplicate discounts are prohibited: The manufacturer is required to provide access to either the MFP or the 340B price, whichever is lower.¹⁸⁷

B. MFP rebate model

BIO commends CMS for proposing that access to the MFP may be provided through an MFP rebate model and urges the Agency to clarify that the proposed fourteen-day period during which an MFP rebate must be paid runs from the date on which the manufacturer has validated eligibility for the rebate.

CMS proposes that a manufacturer may provide access to the MFP by either (1) ensuring that the price paid when acquiring the drug is no greater than the MFP or (2) providing retrospective reimbursement for the difference between the acquisition cost and the MFP.¹⁸⁸ BIO commends this approach.

Generally speaking, the manufacturer of a selected drug must provide access to the MFP to providers and pharmacies with respect to Part B, MA, and Part D beneficiaries.¹⁸⁹ It follows that the manufacturer has no obligation to provide access to the MFP to providers and pharmacies on units that will be furnished or dispensed to individuals who are not Part B, MA, or Part D beneficiaries (MFP-ineligible individuals).

An MFP rebate model is vital because it enables prospective safeguarding against diversion of MFP units to MFP-ineligible individuals. This is essential because the statute does not provide any retrospective

¹⁸⁵ SSA § 1193(a)(3)(B); *see also id.* § 1191(c)(2)(B).

¹⁸⁶ *Id.* § 1193(a)(3)(A); *see also id.* § 1191(c)(2)(A).

¹⁸⁷ *Id.* § 1193(d).

¹⁸⁸ Initial Guidance at 40.

¹⁸⁹ *Id.* § 1193(a)(3); *see also id.* § 1191(c)(2).



mechanism for doing so. For example, the statute does not provide any post-hoc audit right to either the manufacturer or CMS to validate that providers and pharmacies have appropriately furnished or dispensed MFP units. Nor is there any post-hoc dispute resolution mechanism that enables the manufacturer to contest and recover the MFP discount on units that were improperly furnished or dispensed. Likewise, the statute does not grant CMS authority to impose CMPs or other sanctions, such as termination of access to the MFP, on providers and pharmacies that engage in diversion. Under these circumstances, CMS must establish a means to prospectively prevent diversion of MFP units. Authorizing an MFP rebate model is the most logical and practical means of doing so. It provides a mechanism through which the manufacturer can confirm that a unit was in fact furnished or dispensed to an MFP-eligible individual before providing access to the MFP.¹⁹⁰

Absent an MFP rebate model, there would be no way to mitigate against unlimited diversion of MFP units. And this is not a merely theoretical concern. In contrast to the Negotiation Program, the 340B Program, which is generally administered via upfront discounts, features a statutory audit right, a statutory dispute resolution mechanism, and agency authority to impose sanctions, including termination of access to the 340B price.¹⁹¹ Yet even this constellation of statutory safeguards against diversion has proven deeply inadequate to prevent diversion of 340B units.¹⁹² In the face of this well-documented real world experience, it would be patently unreasonable if CMS were to require upfront MFP discounts with no such safeguards. Indeed, doing so would be impermissible, as it would be tantamount to nullifying the express limitation on the obligation to provide access to the MFP only with respect to MFP-eligible individuals.¹⁹³

A rebate model is also the most administratively straightforward means of providing access to the MFP. The rebate model is commonplace in the commercial sector and under Part D, such that an MFP rebate model can be implemented as seamlessly and efficiently as possible and in a manner well familiar to all

¹⁹⁰ As a manufacturer can confirm when it submits its “process for making the MFP available,” Initial Guidance at 32, the minimum necessary Medicare claims data will be used to validate eligibility for the MFP, and reasonable time frames for submission of a request for, validation of eligibility for, and payment of an MFP rebate will be established. Additionally, providers and pharmacies will know at the time that a unit of a drug is furnished or dispensed that the drug is a selected drug and its associated MFP-based cost-sharing. As such, an MFP rebate model will not interfere with timely access by MFP-eligible individuals to MFP-based cost-sharing.

¹⁹¹ PHSA § 340B(a)(5)(C), (d)(2)(B)(v), (3).

¹⁹² See, e.g., Examining HRSA’s Oversight of the 340B Drug Pricing Program: Hearings Before the Subcomm. on Oversight & Investigations of the H. Comm. on Energy & Commerce, 115th Cong. 2–3 (2017) (noting limited oversight against diversion and that between 63 and 82 percent of audited 340B covered entities have been found to be noncompliant with at least one program requirement) (statement of Rep. Tim Murphy), available at <https://www.congress.gov/115/chrgr/CHRG-115hrg26929/CHRG-115hrg26929.pdf>; T. Okon, *Hospitals and for-profit PBMs are diverting billions in 340B savings from patients in need*, Stat News, <https://www.statnews.com/2022/07/07/for-profit-pbms-diverting-billions-340b-savings/> (June 7, 2022); see also PHSA § 340B(a)(5)(B).

¹⁹³ *Whitman v. Am. Trucking Ass’n, Inc.*, 531 U.S. 457, 484 (2001) (an agency may not implement a statute in a manner that “completely nullifies” an otherwise applicable provision).



stakeholders. And CMS has clear legal authority to permit an MFP rebate model, as the statute does not specify how the manufacturer of a selected drug must provide access to the MFP, and, what is more, the statute grants CMS broad discretion to “establish[] . . . procedures to carry out the provisions of [the Negotiation Program], as applicable, with respect to [MFP-eligible individuals].”¹⁹⁴

To ensure smooth integration of the rebate model, and because only pharmacies know the actual acquisition cost (AAC), BIO recommends CMS define the MFP discount using a publicly reported metric, such as wholesale acquisition cost (WAC).

BIO is concerned with the metric CMS is proposing to use when defining the MFP discount, the AAC. CMS proposes that manufacturers that provide access to the MFP using a rebate model will need to provide the pharmacy a discount equal to the difference between the pharmacy’s acquisition cost, or the AAC, and the MFP. Among others, there are concerns with accessibility of the pharmacy’s AAC as it is currently not known to entities beyond the pharmacy. BIO recommends CMS define the MFP discount using a publicly reported metric, such as wholesale acquisition cost (WAC).

To facilitate a functional rebate model, BIO urges CMS to clarify that the proposed fourteen-day period during which an MFP rebate must be paid runs from the date on which the manufacturer has validated eligibility for the rebate.

CMS proposes that the manufacturers provide retrospective reimbursement within fourteen days. But the Initial Guidance is silent on when the clock begins to run. CMS should clarify that the clock begins to run on the date on which the manufacturer has validated eligibility for the rebate, in accordance with commercial sector conventions. In fact, this is the only rational starting point.

If CMS were instead to suggest that the clock begins to run on the date on which the rebate is requested, there would be insufficient time for the manufacturer to confirm that the unit was in fact furnished or dispensed to an MFP-eligible individual before providing access to the MFP—and, more fundamentally, no incentive for a provider or pharmacy to provide any validating Medicare claims data (including the 340B and non-340B claims modifiers discussed in section VI.C). This would render the rebate model completely nugatory, as such data are essential to the rebate model. Alternatively, we believe CMS should require providers to furnish claims level data such that it is required to process an individual claim, including the 340B or non-340B claims modifier as necessary. As CMS notes in its communication to states entitled, “Best Practices for Avoiding 340B Duplicate Discounts in Medicaid,” manufacturer access to claims level data is likely needed for invoice validation.¹⁹⁵ The rebate model is

¹⁹⁴ SSA § 1196(a)(3).

¹⁹⁵ Best Practices for Avoiding 340B Duplicate Discounts in Medicaid, CMS, January 8, 2020. https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/cib010820_1.pdf.



useful only to the extent that it provides a meaningful opportunity to prospectively safeguard against statutorily prohibited diversion of MFP units to MFP-ineligible individuals. As such, the rebate payment clock must begin ticking only after the manufacturer has verified the propriety of the rebate. Any contrary approach would be both plainly irrational and run directly contrary to the clear intent of Congress, which declined to impose any obligation on the manufacturer to provide access to the MFP with respect to an MFP-ineligible individual.¹⁹⁶

To promote efficiency and program integrity and to minimize the burden on interested parties, CMS should adopt a third-party administrator or clearinghouse rebate model.

Finally, BIO strongly urges CMS to utilize a CMS-established third-party administrator (TPA) for the rebate model. By utilizing a TPA, CMS can ensure prompt payment while promoting efficiency and program integrity and minimizing obligations on stakeholders. The CMS-established TPA would also need to serve as a Medicare claims data clearinghouse. To enable manufacturers that choose the rebate option to validate the propriety of MFP rebate invoices, CMS should require all necessary claims level data be shared with the clearinghouse such that it is required to process an individual claim, including the 340B or non-340B claims modifier. The TPA clearinghouse would also be an effective way to ensure non-duplication between the MFP and the 340B program.

C. MFP-340B Duplicate Discounts

To prevent MFP-340B duplicate discounts, BIO urges CMS to condition payment of a claim for reimbursement for a unit of a selected drug on the accurate use of *either* a 340B or a non-340B claims modifier, across Part B, MA, and Part D.

As set forth above, the statute prohibits MFP-340B duplicate discounts.¹⁹⁷ To make this statutory prohibition meaningful, CMS must establish a mechanism that meaningfully allows manufacturers to avoid MFP-340B duplicate discounts across Part B, MA, and Part D.

With respect to Part B, CMS has already taken steps toward establishing such a mechanism. Effective January 1, 2024, all 340B covered entities that submit a Part B claims must use a 340B claims

¹⁹⁶ In the alternative to requiring payment of an MFP rebate within fourteen days of the date on which the manufacturer has validated eligibility for the rebate, CMS could requirement payment of an MFP rebate either (1) within thirty days of the date on which the provider or pharmacy submits all necessary validating Medicare claims data, to be tolled during the pendency of a reasonable dispute resolution process or (2) within 45 days of the date on which the provider or pharmacy submits all necessary validating Medicare claims data. Notably, if the clock were to begin to run before the submission of such data, it would render the rebate model pointless, as the entire point of the model is to enable the manufacturer to validate eligibility for the rebate.

¹⁹⁷ *Id.* § 1193(d) (the manufacturer is required only to offer the lower of the MFP and the 340B price).



modifiers.¹⁹⁸ With respect to Part D, CMS has similarly proposed to require a 340B identifier in prescription drug event (PDE) file, acknowledging that “requiring that a 340B indicator be included on the [PDE] record is the most reliable way to identify drugs that are subject to a 340B discount that were dispensed under Medicare part D,” for purposes of excluding 340B units from the Part D inflation rebate calculation.¹⁹⁹

BIO appreciates these steps, but CMS must take additional steps to make the prohibition of MFP-340B duplicate discounts meaningful. As a start, CMS must require the use of either a 340B modifier or a non-340B modifier, and condition payment of a claim on the accurate use of the applicable modifier. And CMS must implement the same constellation of essential safeguards with respect to MA units. All such safeguards are necessary to ensure that 340B covered entities are properly incentivized to accurately identify 340B units. And such safeguards must be paired with an MFP rebate model to prospectively guard against MFP-340B duplicate discounts, given the absence of a statutory mechanism for retrospectively doing so.²⁰⁰ Any other safeguards necessary to protect against MFP-340B duplicate discounts should be adopted as well.

The need for such protections is readily apparent in light of the long history of improper duplicate discounts in analogous contexts: There continues to be widespread 340B covered entity non-compliance issues with respect to the MDRP-340B duplicate discount prohibition.²⁰¹ The same risk is present with respect to MFP-340B duplicate discount, and CMS must establish a mechanism to guard against them, as the prohibition against MFP-340B duplicate discounts is meaningful only if CMS does so. “An administrative agency cannot abdicate its responsibility to implement statutory standards under the guise of determining that inaction is the best method of implementation.”²⁰²

D. Providing access to the MFP to Part D beneficiaries at the point of sale

BIO concurs with CMS that a manufacturer is not required to provide access to the MFP to Part D beneficiaries at the point of sale *directly*.²⁰³

¹⁹⁸ CMS, Part B Inflation Rebate Guidance: Use of the 340B Modifiers 1 (Dec. 20, 2022), available at <https://www.cms.gov/files/document/part-b-inflation-rebate-guidance340b-modifierfinal.pdf>.

¹⁹⁹ CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum 18 (Feb. 9, 2023), available at <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>.

²⁰⁰ See § VI.B *supra*.

²⁰¹ See, e.g., Government Accountability Office, *Drug Discount Program: Federal Oversight of Compliance at 340B Contract Pharmacies Needs Improvement* (2018), available at <https://www.gao.gov/assets/gao-18-480.pdf>; see also PHSA § 340B(a)(5)(A).

²⁰² *United States v. Markgraf*, 736 F.2d 1179, 1183 (7th Cir. 1984).

²⁰³ Initial Guidance at 31.



In the Initial Guidance, CMS correctly recognizes that access to the MFP must be provided to Part D beneficiaries at the point of sale through PDPs or MA-PDPs, as opposed to the manufacturer (as a literal reading of the statute might suggest).²⁰⁴ This is because it is impossible for a manufacturers to provide access to the MFP to Part D beneficiaries at the point of sale directly because they are not a party to the transaction at the point of sale. Rather, the point-of-sale transaction is among the Part D beneficiary, the pharmacy, and the plan or its PBM. Not only are manufacturers not a party to the transaction at the point of sale, but they are also typically not even in privity of contract with the point-of-sale pharmacy (and may also not even be in privity of contract with the plan or its PBM). As such, the only rational way to operationalize the statutory directive is for CMS to establish a pathway by which the MFP is passed through to Part D beneficiaries by those that are parties to the point-of-sale transaction. Therefore, BIO concurs with CMS’s clarification that access to the MFP by Part D beneficiaries at the point of sale will be effectuated through plans, not manufacturers.

E. Application of the MFP Across Dosage Forms and Strengths

We request that CMS simplify its proposed approach and address concerns with its proposed methodology.

In section 60, CMS proposes a complicated set of comparisons for purposes of creating a single proposed MFP for each drug for negotiation purposes. BIO understands the agency’s application of the statutory directive to create a “maximum fair price across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug.” However, the agency’s decision, discussed above to treat products that are the subject of discrete NDAs as the same drug because they have the same active moiety, unnecessarily compounds the complexity of this effort. In many cases, products requiring significantly different routes of administration treat different conditions or have different clinical profiles—which results in a requirement for discrete NDAs to establish that the use of these therapies is safe and effective. In addition, drugs with different routes of administration may have substantially different manufacturing costs.

Thus, while BIO understands what the agency was attempting to accomplish in the system it has proposed for resolving the calculation of MFP across all dosage forms and strengths, the complexity of the system is compounded by CMS’ desire to include, in a single calculation, products with multiple routes of administration that will often be approved under multiple NDAs as separate drugs. The calculation also relies upon standardized concepts of 30-day equivalent supply, which may or may not have a true equivalence, especially for any products with some formulations dosed once via injection to

²⁰⁴ SSA § 1193(a)(3).



last a longer period of time which may not be standardized across all clinical practice—and may differ markedly from oral formulations for the same chemical. The complicated equation CMS has established may not be able to adequately resolve these differences when calculating a standardized MFP across all forms and strengths of particular chemical compounds—and it need not do so for products approved under separate NDAs that should be treated as different drugs for purposes of MFP calculations.

BIO urges CMS to simplify MFP calculations by following the statutory language of the IRA and attempt to create a single MFP only for dosage forms of each drug that are identified by reference to the same NDA or BLA. Products that are separately approved should be treated as separate drugs. This will resolve much of the unnecessary complexity in the agency’s proposed calculations described in section 60.

In addition, BIO is concerned that the last step of the 10-step process CMS has outlined will create an additional round of price cuts on dosage forms and strengths which cost more than other dosage forms and strengths for the same product for purposes of these calculations. By selecting a single ceiling price for the MFP and then comparing it differentially to the NDC9 level ceiling prices for the different dosage form and strengths of products, CMS is effectively undermining its own “single” MFP ceiling. Products which cost more at the NDC9 level than the dosage form and strength level calculated in section 60.2.2 and 60.2.3 would be subjected to two rounds of cuts, one during the process outlined in section 60.5 and again during the negotiation process itself. This undermines the creation of a “single” MFP since the different dosage forms and strengths are not equally subjected to the two rounds of cuts. This could potentially penalize more expensive dosage forms and strengths and undermine the ability of manufacturers to continue to provide these products. Moreover, the differential impact of the CMS methodology across dosage forms and strengths could also result in inequitable patient cost sharing.

In sum, BIO urges CMS to consider ways to simplify its methodology for applying the MFP across different dosage forms and strengths to avoid these distortions. As noted, some of these issues could be mitigated if CMS treats products which are separately approved as separate drugs. In addition, BIO believes that the agency has the authority to apply the MFP using more simplified units of measure than the 30-day equivalent methodology CMS has proposed.

F. The Date on Which a Generic or Biosimilar Is Marketed and the Date on Which CMS Determines That a Generic or Biosimilar Has Been Marketed

It is imperative that CMS abandon its bona fide marketing standard. This standard for determining the date of marketing of a generic or biosimilar is incompatible with the statute and contrary to sound public policy. CMS should instead adopt a standard that consistently designates the MDRP “market



date” as both the date on which a generic or biosimilar is marketed *and* the date on which CMS determines that a generic or biosimilar has been marketed.

The statute anchors multiple important provisions to either (1) the date on which a generic or biosimilar is marketed or (2) the date on which CMS determines that a generic or biosimilar is marketed.

With respect to the former date, a drug or biologic may be selected for negotiation only if, by the selected drug publication date, it is a qualifying single source drug—which excludes a drug or biologic with respect to which a generic or biosimilar is marketed.²⁰⁵ In addition, a biologic subject to a delay in selection for negotiation is rendered ineligible for selection for negotiation if a biosimilar is marketed by the date that is two years what otherwise would have been the selected drug publication date.²⁰⁶ And a biologic may not be subject to such a delay if more than one year has passed since the biosimilar was licensed and the biosimilar is not marketed.²⁰⁷

With respect to the latter date, most notably, a selected drug ceases to be subject to the MFP at the start of the year that is “at least 9 months after the date on which [CMS] determines that at least one generic or biosimilar has been marketed.”²⁰⁸ In addition, a drug or biologic ceases to be subject to negotiation if, by the end of the negotiation period, CMS determines that a generic or biosimilar has been marketed;²⁰⁹ and a non-compliant manufacturer of a selected drug subject to an ongoing excise tax ceases to be subject to such tax on the date on which CMS determines that a generic or biosimilar has been marketed.²¹⁰

In either case, the determination of the date of marketing of a generic or biosimilar is of enormous consequence throughout the program. CMS has stated its intent to use an ill-defined and complicated process to make what is in fact an entirely straightforward determination. CMS intends to review PDE data to determine whether a generic or biosimilar is marketed under a “bona fide marketing” standard that reflects CMS’s subjective assessment of whether the degree of utilization of the generic or biosimilar represents “robust and meaningful competition.”²¹¹

²⁰⁵ *Id.* § 1192(e)(1)(A)(iii); (B)(iii). The statute refers to a generic or biosimilar that is both approved or licensed and marketed. We focus only on the latter because the date of marketing should never fall before the date of approval or licensure.

²⁰⁶ *Id.* § 1192(f).

²⁰⁷ *Id.* § 1192(f)(2)(D)(iii).

²⁰⁸ *Id.* § 1192(c)(1) (emphasis added).

²⁰⁹ *Id.* § 1192(c)(2).

²¹⁰ Internal Revenue Code (IRC) § 5000D(b)(1)(B).

²¹¹ Initial Guidance at 67. BIO notes that, in some cases, the Initial Guidance does not specify whether the Agency intends to use the bona fide marketing standard to determine the date of marketing. In particular, it is unclear whether CMS intends to use such standard with respect to provisions regarding delay in the selection of a biologic for negotiation. If CMS intends to use an alternative standard with respect to such provisions, it should clearly articulate such alternative and subject it to public comment.



CMS’s approach is deeply problematic for myriad reasons. Foremost is that the bona fide marketing standard is contrary to the plain language of the statute: CMS’s standard is not rationally related to the actual date of marketing. As a definitional matter, marketing is “[t]he act[] . . . of bringing or sending a product or commodity to market.”²¹² As such, once the “action of buying or selling” has occurred, a product has necessarily been “marketed.”²¹³

CMS itself has long recognized that the date on which a product is “marketed” is an objective point-in-time determination of the date on which it is made available for sale in the commercial marketplace—including in the course of implementing other provisions of the IRA as well as under the Part D program which will source the data on which CMS intends to rely in effectuating its bona fide marketing standard. Mere months ago, CMS proposed to determine when a product is “marketed” for purposes of the IRA’s Part D inflation rebates by reference to the “market date” that the manufacturer must report under MDRP.²¹⁴ In turn, under MDRP, CMS has long defined the “market date” of a product by reference to the date on which the product entered commercial distribution, consistent with the plain language definition of “marketed.”²¹⁵ And, under the Part D program, which will source the PDE data on which CMS intends to rely in effectuating its bona fide marketing standard, CMS has recognized that the date on which a product is “release[d] onto the market” triggers certain coverage-related obligations²¹⁶—which by necessary implication means that CMS will have already recognized that a product has been released onto market by the time such coverage-related obligations yield PDE data showing utilization of the product.

²¹² Oxford English Dictionary, Definition of Marketing,
<https://www.oed.com/view/Entry/114186?rskey=36dfg4&result=2&isAdvanced=false#eid> (last visited Mar. 19, 2023).

²¹³ *Id.*

²¹⁴ CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1860D-14B of SSA, and Solicitation of Comments, § 40.3 (Feb. 9, 2023), *available at* <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>; FDA, National Drug Code Directory (July 22, 2022), *available at* <https://www.fda.gov/drugs/drug-approvals-and-databases/national-drug-code-directory#:~:text=Marketing%20start%20date%20is%20the,no%20longer%20in%20commercial%20distribution>. With respect to the IRA’s Part B inflation rebate, CMS proposed to determine when a product is “marketed” by reference to the “date of first sale” that the manufacturer must report for ASP purposes, which likewise is an objective point-in-time determination. CMS, Medicare Part B Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1847A(i) of the Social Security Act, and Solicitation of Comments, § 50.3 (Feb. 9, 2023), *available at* <https://www.cms.gov/files/document/medicare-part-b-inflation-rebate-program-initial-guidance.pdf>.

²¹⁵ 83 Fed. Reg. 12,770, 12,784 (Mar. 23, 2018) (MDRP National Rebate Agreement); *see also* 42 CFR 447.502.

²¹⁶ CMS requires that Part D plan sponsor P&T committees “make a reasonable effort to review a new FDA approved drug product (or new FDA approved indication) within 90 days of its release onto the market and . . . make a decision on each new FDA approved drug product (or new FDA approved indication) within 180 days of its release onto the market, or a clinical justification will be provided if this timeframe is not met.” Prescription Drug Benefit Manual, ch. 6 § 30.1.5 (emphasis added).



CMS should not supplant wholesale the statute’s objective point-in-time “marketed” standard with an extra-statutory standard based on the Agency’s subjective judgment of sufficiency of utilization.²¹⁷ Such judgment is immaterial to whether a product is in fact marketed—i.e., is available to be bought and sold in the commercial marketplace.

Notably, Congress well knows how to statutorily impose a “bona fide” standard in the drug pricing context. Congress expressly established such a standard when amending the MDRP statute in 2010 to specify that only “bona fide” service fees are exempt from the calculation of AMP.²¹⁸ By contrast, Congress chose not to establish such a bona fide standard here. “[W]here Congress knows how to say something but chooses not to, its silence is controlling.”²¹⁹

CMS’s extra-statutory bona fide marketing standard has vast legal implications. For example, as noted above, the date on which CMS determines that a generic or biosimilar has been marketed determines when the MFP terminates.²²⁰ As such, through the bona fide marketing standard, CMS is effectively claiming for itself limitless discretion to prevent the MFP from timely (if ever) terminating, notwithstanding the fact that a generic or biosimilar has in fact come to market, based on the Agency’s subjective assessment of whether PDE data show that the generic or biosimilar is utilized sufficiently. In addition, CMS is implicitly claiming for itself authority to re-institute an MFP after an MFP has been terminated, if the Agency concludes based on PDE data that utilization of the generic or biosimilar ceases to be “robust and meaningful.”²²¹

Such policies are completely untethered to anything in the text or structure of the statute and run directly contrary to Congress’s intent to allow market-based competition to govern where a generic or biosimilar has come to market to compete with a drug or biologic.²²² The Agency’s approach is therefore patently unlawful. “[N]either federal agencies nor the courts can substitute their policy judgments for those of Congress.”²²³ CMS’s effort to do so here is “effectively the introduction of a whole new regime of regulation,” which “is not the one that Congress established.”²²⁴

The Agency’s unlawful standard also necessarily yields an inaccurate determination of when a generic or biosimilar was marketed. The Agency’s reliance on PDE data guarantees that there will be a time lag

²¹⁷ It is unclear, for example, whether CMS expects a generic or biosimilar to capture and maintain a certain percentage of the market.

²¹⁸ SSA § 1927(k)(1)(B)(i)(II) (as amended by Pub. L. No. 111–148, § 2503(a) (2010)).

²¹⁹ *Animal Legal Def. Fund v. U.S. Dep’t of Agric.*, 789 F.3d 1206, 1217 (11th Cir. 2015).

²²⁰ SSA § 1192(c)(2).

²²¹ See Initial Guidance at 67.

²²² See, e.g., SSA § 1192(c)(1).

²²³ *Brown & Williamson Tobacco Corp. v. FDA*, 153 F.3d 155, 176 (4th Cir. 1998), *aff’d*, 529 U.S. 120 (2000).

²²⁴ *MCI Telecomms. Corp. v. Am. Tel. & Tel. Co.*, 512 U.S. 218, 114 (1994).



between the actual date of marketing and the date of CMS's determination because it takes time for sales to be reflected in PDE data. Indeed, CMS's long-standing policy requiring Part D plan sponsors to determine whether to add a newly approved drug to their formulary within 180 days of its release onto the market ensures that the PDE data will not accurately reflect when the drug came to market. Many Part D plan sponsors will not add a newly approved drug to their formulary until the 180-day mark, and, thus, the first six months of PDE data following the market entry of the drug will necessarily reflect only very limited uptake.²²⁵ And some plan sponsors may choose not add the drug to their formulary at all. In addition, even where plan sponsors add the drug to their formulary, widespread uptake of a new product does not occur overnight. After a new product is made available for sale, providers and patients typically transition to such product gradually as they become increasingly familiar with its benefits relative to pre-existing alternatives.²²⁶ Such a product is in fact marketed during this uptake period, but CMS's standard ignores this fact and focuses instead on whether the product is adequately utilized, in contravention of the statutorily mandated standard.²²⁷ Such shifts in utilization patterns over time do not mean that the market is not working as intended.

The Agency compounds these concerns with its intent to review PDE data only once per month for purposes of determining when the MFP terminates.²²⁸ The Agency's approach virtually always ensures that there will be a lag between the actual date of marketing and the date of CMS's determination. This poses a significant concern with respect to when the MFP terminates. If there is a lag of even a single day between the actual date of marketing and the date of CMS's determination, a selected drug can be subject to the MFP for a full additional year. For instance, if, on April 1, a generic or biosimilar is in fact marketed on April 1, but CMS's determination of this fact is deferred until April 2, the selected drug is subject to the MFP for a full year longer than if CMS's determination had not been deferred.

It is imperative that CMS abandon its unlawful and ill-advised standard and instead adopt as its standard the "market date" reported under MDRP. The MDRP "market date" standard should be used for identifying *both* the date on which a generic or biosimilar is marketed *and* the date on which CMS determines that a generic or biosimilar has been marketed.

Under MDRP guidance, "market date" is "the earliest date the drug was first marketed under the application number by any labeler."²²⁹ Manufacturers report this date when reporting MDRP pricing

²²⁵ While plan enrollees may access a non-formulary drug via an exceptions process, access may not be immediate under such process; moreover, exception processes typically yield only a very small volume of utilization.

²²⁶ See A. Lubby, Factors affecting the uptake of new medicines: a systematic literature review, 14 BMC Health Services Research 469 (2014) (describing the various factors that affect early uptake of new medicines).

²²⁷ Other examples of deficiencies in CMS's approach include circumstances where low utilization is driven by uncontrollable factors such as supply shortages.

²²⁸ Initial Guidance at 62.

²²⁹ CMS, MDRP Data Guide § 5.15 (Apr. 2022).



data. As such, the MDRP “market date” is a familiar construct to both CMS and manufacturers, and carries the additional benefit of ensuring consistency across MDRP and the Negotiation Program. And, unlike the “date of first sale” used for ASP reporting purposes, the MDRP “market date” is available for generics and biosimilars without regard to whether they are subject to ASP reporting.²³⁰

It is particularly critical that the Agency equate the date on which CMS determines that a generic or biosimilar has been marketed with the MDRP “market date” because, as noted above, the difference of a single day in the date of CMS’s determination can result in the MFP being extended for a full additional year. Failing to do so would have a dramatic chilling effect on the development of generics and biosimilars. Manufacturers would be seriously disincentivized against investing in the development of such products if there is a risk that they would be forced to compete with the MFP for an unduly extended period of time. This, in turn, would defeat Congress’s objective of encouraging the development of generic and biosimilar market competitors.

For all of these reasons, we strongly oppose CMS’s extra-statutory bona fide marketing standard, and strongly urge CMS instead to adopt the MDRP “market date” as a uniform standard for identifying both the date on which a generic or biosimilar is marketed and the date on which CMS determines that a generic or biosimilar has been marketed.

VII. Other Issues

A. Selected Drugs and Inflation Rebates

BIO urges CMS to clarify that selected drugs are not subject to an inflation rebate.

In its Initial Guidance, CMS solicits comment on the application of Part B and Part D inflation rebates to selected drugs.²³¹ Notably, CMS asserts: “The Part B and Part D inflation rebate programs apply to selected drugs, regardless of the status of the drug as a selected drug. Alternatively said, whether a drug is a selected drug will have no bearing as to whether the drug is also subject to the Part B and Part D inflation rebate programs.”²³² This assertion is incorrect. BIO asks CMS to clarify a selected drug is not subject to an inflation rebate.

²³⁰ The “date of first sale” is reported only for products subject to ASP reporting, and thus may not be available for all generics and biosimilars whose marketing is implicated by the Negotiation Program. By contrast, the “market date” reported under MDRP is more broadly reported and is thus the superior metric to use. See CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1860D-14B of Social Security Act, and Solicitation of Comments, (Feb. 9, 2023), <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>.

²³¹ Initial Guidance at 71.

²³² *Id.*



By statute, the Part B inflation rebate calculation is based in relevant part on the amount by which “106 percent of the amount determined under paragraph (4) of [section 1847A(b) of the SSA] for [a part B rebatable drug] during the calendar quarter . . . exceeds . . . the inflation-adjusted payment amount . . . for such part B rebatable drug during the calendar quarter.”²³³

Importantly, the circumstances under which an amount is “determined” under paragraph (4) is dictated by section 1847A(b)(1) (paragraph (1)).²³⁴ Specifically, paragraph (1) dictates a payment amount of, “in the case of a single source drug or biological . . . , 106 percent of the amount determined under paragraph (4) or in the case of such a drug or biological product that is a selected drug . . . , with respect to a price applicability period . . . , 106 percent of the maximum fair price . . . applicable for such drug and a year during such period.”²³⁵

In other words, the payment amount for a selected drug is determined under paragraph (1), and such payment amount is determined without regard to paragraph (4). Rather, it is only the payment amount for a non-selected drug that is determined under paragraph (4).

It necessarily follows that the Part B inflation rebate calculation has no application to a selected drug. With respect to such a drug, there is no amount “determined under paragraph (4),” and therefore Part B inflation rebates have no applicability.

This is not surprising. There is no policy reason for Congress to apply inflation rebates to selected drugs. A manufacturer should not be obligated to pay an inflation rebate on a selected drug because Medicare expenditures on a selected drug are already constrained by the maximum fair price.²³⁶ Thus, with respect to a selected drug, Medicare is shielded from the increase in expenditures occasioned by a price increase that outpaces inflation that an inflation rebate is intended to address. Medicare does not need to be made whole on account of such a price increase, and, thus, no inflation rebate should be due.

For all of these reasons, CMS should clarify that a selected drug is not subject to an inflation rebate.

²³³ SSA § 1847A(i)(3) (emphasis added).

²³⁴ See *id.* § 1847A(b)(1).

²³⁵ *Id.* § 1847A(b)(1)(B) (emphasis added).

²³⁶ *Id.* §§ 1847A(b)(1)(B); 1860D-2(d)(1)(D).



B. MFP and ASP

BIO urges CMS to amend its regulatory definition of “unit” to exclude MFP units from the ASP calculation.

By statute, MFP units are included in Best Price.²³⁷ Sales included in Best Price are also generally included in ASP.²³⁸ Thus, in the ordinary course, MFP units would be included in the ASP calculation. But the inclusion of MFP units in the ASP calculation would have vast and dire consequences for patient access.

The inclusion of MFP units in the ASP calculation would increasingly deflate ASP over time. As a result, ASP-based provider reimbursement would increasingly become inadequate to cover providers’ acquisition costs. Eventually, providers would be left financially underwater if they were to furnish a selected drug to an MFP-ineligible individual, creating a very real risk that providers would no longer furnish such drugs to such individuals. And this vital threat to patient access to necessary medicines would be far-reaching. ASP is a reimbursement benchmark commonly used by non-Part B payers with respect to Part B drugs. As such, although Part B reimbursement for selected drugs will not be based on ASP, this would negatively affect countless individuals insured by non-Part B payers.

Fortunately, CMS has clear legal authority to prevent this. The ASP statute unambiguously confers on CMS broad authority to define “unit” for purposes of the ASP calculation “as . . . [CMS] determines appropriate.”²³⁹ CMS undoubtedly may exercise such authority to exclude MFP units from the ASP calculation to avoid the patient access concern described above.

The legislative history of the ASP statute makes abundantly clear that Congress intended for CMS to exercise such discretion in this way in precisely this sort of circumstance. When Congress delegated CMS the authority to define “unit” for purposes of the ASP calculation, it specifically stated that it was doing so to allow for the exclusion of “those sales that do not reflect market prices” from ASP.²⁴⁰ By definition, MFP units do not reflect market prices.

There is also clear Agency precedent for excluding units that do not reflect market prices from the ASP calculation. In 2005, CMS carved Competitive Acquisition Program (CAP) units out of the ASP exclusion by excluding such units from the “unit” definition.²⁴¹ In doing so, CMS noted that ASP and CAP prices

²³⁷ *Id.* § 1927(c)(1)(C)(ii)(V).

²³⁸ *See id.* § 1847A(c)(2)(A); *see also* 42 C.F.R. § 414.804(a)(1), (4)(i).

²³⁹ SSA § 1847A(b)(2)(B).

²⁴⁰ *See* H.R. Rep. No. 108-391, at 587–88 (2003).

²⁴¹ 70 Fed. Reg. 39,021, 39,077 (Jul. 6, 2005); *see also* 74 Fed. Reg. 61,738, 61,915 (Nov. 25, 2009).



were “intended to be alternatives to each other” and, thus, CAP units should not be included in the ASP calculation.²⁴²

Identical reasoning supports excluding MFP units from the ASP calculation. MFP units do not reflect market prices: Rather, the MFP is a government-set price. Further, the MFP functions as an alternative to ASP: Part B will reimburse providers based on the MFP in lieu of ASP.²⁴³

For all these reasons, sound policy dictates that CMS exclude MFP units of selected drugs from the ASP calculation. BIO urges CMS to do so well in advance of the first IPAY to avoid any confusion and potential destabilization on non-Medicare markets once MFPs go into effect for the first set of selected drugs.

C. Civil Monetary Penalties (CMPs)

BIO urges CMS to proceed with caution on the implementation of CMPs as proposed given the ambitious timelines in the statute and to allow manufacturers a reasonable time period to cure deficiencies before CMPs are imposed. And in no case should the Agency impose a CMP prior to finalization of relevant regulations.

Under the IRA, CMS can impose CMPs on drug manufacturers for the following infractions related to the Part D Drug Negotiation program:

- **Refusing Access to MFP Price:** CMS will impose a CMP of 10 times the amount equal to number of units of drug furnished multiplied by the difference between the price for such drug made available to MFP-eligible entities on a Primary Manufacturer of a selected drug that has entered into an Agreement with CMS and fails to provide access to a price that is less than or equal to the MFP to MFP-eligible individuals dispensed the selected drug to pharmacies, mail order services, or other dispensers with respect to MFP-eligible individuals who are dispensed the selected drug or to hospitals, physicians, or other providers or suppliers that furnish or administer the selected drug to MFP-eligible individuals.
- **Failure to Comply to Requirements:** Any Primary Manufacturer of a selected drug that has entered into an Agreement with that fails to comply with requirements determined by CMS to be necessary for the purposes of administering the Negotiation Program and monitoring

²⁴² 78 Fed. Reg. at 61,915.

²⁴³ SSA § 1847A(b)(1)(B).



compliance with the Negotiation Program will be subject to a CMP of \$1,000,000 for *each day* of such violation.

- **Provision of False Information:** If CMS determines that any manufacturer knowingly provides false information under the procedures to apply the aggregation rule for the Small Biotech Exception, such manufacturer shall be subject to a CMP equal to \$100,000,000 for each item of such false information. Likewise, if CMS determines that any Biosimilar Manufacturer knowingly provides false information under the procedures to apply the aggregation of the Biosimilar Delay, the manufacturer shall be subject to a CMP equal to \$100,000,000 for each item of such false information.

CMS will provide notice to the manufacturer with information regarding the CMP in accordance with section 1128A of the Act, including the option to either pay the CMP or to request a hearing as outlined in section 1128A. The CMP notice will include: Basis for the CMP; CMP amount due; Deadline for the manufacturer to respond with a hearing request or submit the CMP payment; Method to submit CMP payment(s); and Information on the right to request a hearing

The manufacturer will have 60 days from the date of receipt of the CMP notice to request a hearing—If the manufacturer does not request a hearing within 60 days, the CMP will be considered due on day 60 following the date of receipt of the CMP notice.

BIO urges CMS to proceed with caution on the implementation of CMPs as proposed. By any recognition, the time frames in statute for implementation of myriad sweeping changes in multiple parts of the Medicare program are ambitious. To make analogies to another program, BIO reminds CMS that a final rule to impose CMPs on drug manufacturers as part of the 340B program in 2017 was delayed multiple times. Although the 2017 Final Rule was scheduled to take effect on March 6, 2017, HRSA delayed the implementation of the rule multiple times. The Agency ultimately postponed the effective date of the rulemaking until July 1, 2019, to allow for “necessary time to consider more fully the substantial questions of fact, law, and policy identified by the Department during its review of the rule.”

We similarly urge CMS to proceed cautiously with the imposition of CMPs on drug manufacturers and urge all stakeholders to work in good faith to comply with the statutory requirements of data reporting. To this end, we request that CMS send a notice of intent to impose a CMP and a reasonable period to cure the deficiency and/or to dispute the basis for the CMP, before any imposition of a CMP. The IRA imposes a tremendous amount of data reporting on drug manufacturers and puts them at risk for significant financial penalties. It will take time for manufacturers, especially small manufacturers, to comply in good faith with all the necessary data collection requests in the first years of the Negotiation program. And in no case should the Agency impose a CMP prior to finalization of relevant regulations.



D. Negotiation Program Agreement

BIO urges CMS to ensure that the text of the Negotiation Program Agreement is made available for public comment at least sixty days in advance of the first selected drug publication date. Further, CMS should abandon its “Primary Manufacturer” and “Secondary Manufacturer” construct as part of the Agreement as it is impracticable and has no legal basis.

The Initial Guidance states that the Agency will make “reasonable efforts” to make the final text of agreement available to the public before the first selected drug publication date.²⁴⁴ It is imperative that CMS make the text of the agreement available for public comment and do so well in advance of when manufacturers will be required to execute the agreement.

Advance notice of, and an opportunity comment on, the precise content of the Negotiation Program Agreement is vital because manufacturers are subject to CMPs of \$1 million dollars per day for a violation of a terms of the agreement.²⁴⁵ What is more, manufacturers that decline to enter into the Negotiation Program Agreement are subject to punitive excise taxes, such that manufacturers are effectively compelled to enter into the agreement.²⁴⁶ Under these circumstances, it is imperative that CMS provide advance notice of, and an opportunity to comment on, the exact terms of the Negotiation Program Agreement. Manufacturers must be reasonably apprised of the specific obligations to which CMS proposes they be subject, and have reasonable opportunity to comment thereon, when compliance is enforced via such extraordinary sanction.

Advance notice is necessary at a minimum because manufacturers may need lead time to establish new processes in order to be prepared to comply with the terms of the agreement. CMS cannot put manufacturers in the untenable position of being subject to sanction for failing to comply with requirements that they cannot fulfill because the Agency did not supply adequate advance notice. Courts have long recognized that “[i]mpossible requirements imposed by an agency are performe unreasonable” and therefore arbitrary and capricious.²⁴⁷

We also reinforce our earlier comments regarding CMS’s proposal to hold a “Primary Manufacturer” responsible for submitting applicable information concerning a “Secondary Manufacturer.” CMS also proposes, among other things, to require that “Primary Manufacturers” ensure that “Secondary Manufacturers” make the MFP available to MFP-eligible entities individuals and other entities, and CMS would impose CMPs on “Primary Manufacturers” for noncompliance by “Secondary Manufacturers.” We

²⁴⁴ Initial Guidance at 27.

²⁴⁵ SSA § 1197(c).

²⁴⁶ IRC § 5000D(b)(1)(A).

²⁴⁷ *All. for Cannabis Therapeutics v. DEA*, 930 F.2d 936, 940 (D.C. Cir. 1991).



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urge CMS to abandon its proposed requirements under this “Primary Manufacturer” and “Secondary Manufacturer” construct. A Primary Manufacturer has no inherent legal authority to compel a Secondary Manufacturer to act or not act.

E. Patient Access and Part D Plan Formulary Placement

CMS should take steps to protect patient access to needed therapies in all Medicare Part D Plans.

By statute, Part D plans must place selected drugs on their formularies.²⁴⁸ BIO recommends that CMS clarify how it will ensure robust beneficiary access to needed therapies, including selected drugs, and asks CMS to ensure safeguards that allow for diversity across formularies to meet patient needs. CMS should try to minimize class effects from the MFP process that would result in narrower formularies and provide fewer choices to patients. In addition, CMS should monitor plan coverage and tiering design, clinical appropriateness of utilization management policies, cost-sharing levels, and patient out of pocket exposure. BIO encourages CMS to update its oversight of formulary requirements and to re-examine Part D coverage determinations and appeals as well as tiering exceptions.

BIO appreciates this opportunity to provide feedback to CMS on the Initial Guidance. We look forward to continuing to work with the Agency on these important issues. Should you have any questions, please do not hesitate to contact Crystal Kuntz at 202-962-9200 or Ckuntz@bio.org.

Sincerely,

/s/

John Murphy
Chief Policy Officer

A blue ink signature of John Murphy, written in a cursive style.

/s/

Crystal Kuntz
Vice President, Healthcare Policy & Research

A blue ink signature of Crystal Kuntz, written in a cursive style.

²⁴⁸ *Id.* § 1860D-4(b)(3)(l).

Via Electronic Mail

April 14, 2023

Meena Seshamani, M.D., Ph.D.
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**Re: Medicare Drug Price Negotiation Program: Initial Memorandum,
Implementation of Sections 1191 – 1198 of the Social Security Act for Initial
Price Applicability Year 2026, and Solicitation of Comments**

Dear Administrator Seshamani:

Boehringer Ingelheim Pharmaceuticals, Inc. (BI) welcomes the opportunity to submit comments in response to the Centers for Medicare & Medicaid Services' (CMS or the Agency) *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (Guidance).¹ BI adopts and incorporates by reference the comments submitted on the Guidance by the Pharmaceutical Research and Manufacturers of America (PhRMA). We offer the following comments to elaborate and expand on certain issues raised by the Guidance.

BI is a leading research-driven biopharmaceutical company committed to innovation in areas of high unmet medical need. Accordingly, BI has a significant interest in CMS's implementation of the Inflation Reduction Act (IRA). While BI supports the goal of ensuring patient access to affordable, life-enhancing medicines, it has significant concerns relating to aspects of the Guidance, including concerns that it imposes impracticable—even impossible—deadlines and processes.

1. Both the Administrative Procedure Act and the Medicare Statute Require Notice and Comment Rulemaking on All Aspects of the Guidance.

As an initial matter, CMS was required to go through notice and comment rulemaking in issuing the Guidance. Under both the Administrative Procedure Act (APA) and Medicare statute, the legal effect of the Guidance drives whether notice and comment, and other rulemaking requirements, are required. Under the APA, agency action that “purports to impose legally binding obligations or prohibitions on regulated parties—and that would be the basis for an enforcement action for violations of those obligations or requirements” must be promulgated using notice and comment rulemaking.² Under the Medicare Act, notice and comment is required for any “rule, requirement, or other statement of policy . . . that establishes or changes

¹ Available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

² *Nat'l Mining Ass'n v. McCarthy*, 758 F.3d 243, 251 (D.C. Cir. 2014).

a substantive legal standard governing the scope of benefits, the payment for services, or the eligibility of individuals, entities, or organizations to furnish or receive services or benefits under [the Medicare statute].”³ The Supreme Court has made clear that the requirement to undergo notice and comment turns on “the contents of the agency’s action, not [its] label.”⁴ Here, the Guidance easily meets either standard, since it purports to impose legally binding obligations on manufacturers, with noncompliance triggering civil monetary penalties (CMPs) and excise taxes.

The IRA’s references to “guidance” and “program instruction” do not displace these notice and comment requirements.⁵ If Congress wishes to supplant such requirements, it must do so expressly. For example, courts have looked to whether the operative statute “present[s] a specific directive to adopt procedures other than those of the APA” or expressly exempts agency action from the APA.⁶ The IRA does neither. Indeed, the IRA does not say that “guidance” or “program instructions” may be issued notwithstanding any other provision of law. “[W]hen two statutes are capable of co-existence, it is the duty of the courts, absent a clearly expressed congressional intention to the contrary, to regard each as effective.”⁷ Accordingly, CMS has erred by not proceeding via notice and comment rulemaking under the APA and Social Security Act and by dispensing with the safeguards those Acts provide.

CMS’s failing is particularly acute with respect to section 30 on “Identification of Selected Drugs for Initial Price Applicability Year 2026,” which CMS has issued as immediately effective. Not only has that section been issued as final, but CMS has declined, without any adequate explanation, to take comment on that section. Thus, manufacturers have not had, and will never have, an opportunity to be heard before CMS regarding CMS’s position on critical issues with respect to how drugs and biological products will be selected for IPAY 2026. These issues include, but are not limited to:

- CMS’s position that it will identify a “qualifying single source drug” (QSSD) eligible for negotiation by aggregating drugs by active moiety and biological products by active ingredient, inclusive of products that are marketed under different New Drug Applications (NDAs)/Biologics License Applications (BLAs) held by the same company;
- CMS’s position that it will consider a generic drug or biosimilar biological product to be marketed when prescription drug event (PDE) data reveals that the manufacturer has engaged in so-called “bona fide” marketing, despite the fact that the statute lacks the “bona fide” limitation and this position conflicts with the plain meaning of “marketed”;
- CMS’s apparent intent to exclude from the orphan drug exclusion active moieties or ingredients with more than one orphan designation or approved indication outside the designation across the sponsor’s NDAs or BLAs;
- CMS’s narrow view of plasma-derived products that are exempt from the QSSD definition; and

³ 42 U.S.C. § 1395hh(a)(2), (b)(1); *see also* *Azar v. Allina Health Servs.*, 139 S. Ct. 1804, 1810-11.

⁴ *Allina Health Servs.*, 139 S. Ct. at 1812.

⁵ IRA § 11001(c).

⁶ *See Asiana Airlines v. Federal Aviation Administration*, 134 F.3d 393, 397 (D.C. Cir. 1998); *Mann Constr. v. United States*, 27 F.4th 1138 (6th Cir. 2022).

⁷ *Maine Cmty. Health Options v. United States*, 140 S. Ct. 1308, 1323 (2020).

- CMS's position that that ongoing litigation does not "count" to establish a high likelihood of biosimilar market entry, even in the context of a planned at-risk launch; and
- CMS's imposition of deadlines surrounding the biosimilar "pause."

Had CMS provided an opportunity for comment, BI would have commented on these and other issues presented by section 30.

For the same reasons given above, the decision to issue section 30 without going through notice and comment rulemaking is erroneous. Furthermore, CMS has not shown "good cause" to dispense with notice and comment as to section 30.⁸ CMS relies on the statutory deadlines to say notice and comment would be "impracticable."⁹ However, "[s]tatutory language imposing strict deadlines, standing alone, does not constitute sufficient good cause."¹⁰ Moreover, "[g]ood cause cannot arise as a result of the agency's own delay."¹¹ CMS waited nearly seven months following enactment of the IRA to publish Guidance. CMS is also mistaken that notice and comment would be "contrary to the public interest" and "unnecessary."¹² Instead, the public interest weighs heavily in favor of the opportunity to comment and participate on implementation of sections 1101 and 1102 of the IRA, which create a new program that will affect incentives for research and development of new medicines and uses thereof as well as patient access to needed therapies. And the Guidance is anything but "a routine determination, insignificant in nature and impact, and inconsequential to the industry and to the public."¹³ Finally, the complete lack of any notice and comment opportunity raises serious concerns under the Due Process Clause of the Fifth Amendment to the Constitution.

2. CMS's proposed plan to protect confidential manufacturer information does not adequately protect such information (section 40.2.1).

CMS's reliance on Exemption 4 of the Freedom of Information Act (FOIA) to protect confidential manufacturer information is insufficient to achieve the statutory goal to protect sensitive, proprietary information. In the Guidance, CMS states that it "intends to implement a confidentiality policy that is consistent with existing requirements for protecting proprietary information, such as Exemption 4 of FOIA."¹⁴ Yet CMS's focus on information falling within Exemption 4 of FOIA is not rooted in the statute. The IRA goes beyond Exemption 4. The IRA provides that "[i]nformation submitted to [CMS] under this part by a manufacturer of a selected drug that is proprietary information of such manufacturer (as determined by the Secretary) shall be used only by [CMS] or disclosed to and used by the Comptroller General of the United States for purposes of carrying out this part."¹⁵ Thus, CMS should clarify that any "proprietary

⁸ 5 U.S.C. § 553(b)(3)(B); *see also* 42 U.S.C. § 1395hh(b)(2)(C) (incorporating the APA's good cause exception). The Guidance only invokes the good cause exception with respect to section 30. Any attempt to invoke the good cause exception for other aspects of the Guidance would be untenable, given that CMS is in fact taking comment on them.

⁹ Guidance, at 2.

¹⁰ *Asiana Airlines*, 134 F.3d at 398.

¹¹ *Nat. Res. Def. Council v. Nat'l Highway Traffic Safety Admin.*, 894 F.3d 95, 114 (2d Cir. 2018).

¹² Guidance, at 2.

¹³ *Mack Trucks, Inc. v. EPA*, 682 F.3d 87, 95 (D.C. Cir. 2012) (stating the standard for a determination that notice and comment is "unnecessary").

¹⁴ Guidance, at 29.

¹⁵ SSA § 1193(c).

information” of a manufacturer shall be disclosed to or exclusively used by CMS or the Comptroller General *only* for IRA purposes, and not used or disclosed for any other reason, regardless of whether the requirements of FOIA Exemption 4 (or any other FOIA exemption) are satisfied.

3. CMS should reconsider some of the proposed data use provisions to increase transparency and cooperation with manufacturers (section 40.2.2).

The data use limitations CMS seeks to impose on manufacturers in the program undermine transparency and pose practical challenges for manufacturers. In the Guidance, CMS contends that manufacturers will not be permitted to “disclose to the public any information in the initial offer or any subsequent offer by CMS, the ceiling price contained in any offer, or any information contained in any concise justification provided with an offer.”¹⁶ CMS asserts that restrictions on disclosure of negotiation information are “in furtherance of the statutory instruction that CMS develop a process that aims to achieve the lowest MFP for each selected drug.”¹⁷ The Guidance, however, does not explain how these restrictions would achieve this goal. To the contrary, such a lack of transparency undermines public confidence in the negotiation process. While CMS would permit the disclosure of negotiation information “as may be required by applicable state or federal law,”¹⁸ there are instances where manufacturers will have important business reasons to share such information (e.g., during certain partnership or licensing negotiations). CMS should abandon this proposed restriction.

According to the Guidance, CMS will require manufacturers to destroy “all information the Primary Manufacturer receives during the negotiation period from CMS . . . within 30 days of a determination by CMS that the drug or biologic no longer qualifies as a selected drug.”¹⁹ This requirement is not justified. In the Guidance, CMS asserts that “these policies will increase the chances of effective and successful negotiation in furtherance of the statutory instruction that CMS develop a process that aims to achieve the lowest MFP for each selected drug.”²⁰ Yet, to support this requirement, CMS points to statutory language that “the manufacturer complies with requirements determined by the Secretary to be necessary for purposes of administering the program and monitoring compliance with the program.”²¹ The Guidance does not explain why or how the destruction of negotiation data potentially years after an MFP has gone into effect is “necessary” to administer the program. Accordingly, we urge CMS to withdraw this provision of the Guidance.

Moreover, the Guidance does not address the challenges and costs of complying with these requirements. To comply with contractual obligations to Secondary Manufacturers, Primary Manufacturers may have to share certain data elements. Furthermore, particularly in the early years of the program, manufacturers may need to share information with various external partners, such as consultants, and a wide array of stakeholders within the company to effectively carry out negotiations with CMS. To facilitate the deletion of all information within 30 days, manufacturers may be required to set up costly data rooms or restrict the parties involved in the

¹⁶ Guidance, at 30.

¹⁷ *Id.*

¹⁸ *Id.*

¹⁹ *Id.*

²⁰ *Id.*

²¹ SSA § 1193(a)(5).

negotiation program to a detrimental extent. BI urges CMS to remove the 30-day deadline to destroy information. At the very least, we encourage CMS to create a process where manufacturers can petition for extensions when necessary.

4. CMS should commit to collaborating with manufacturers to provide the MFP to eligible individuals (section 40.4).

The onerous requirements CMS seeks to impose on manufacturers to ensure they are providing the MFP to eligible individuals are unjustified and unworkable. In section 40.4, CMS states that it intends to “require that Primary Manufacturers provide access to the MFP in one of two ways: (1) ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP; or (2) providing retrospective reimbursement for the difference between the dispensing entity’s acquisition cost and the MFP.” CMS has stated that manufacturers must ensure that dispensing entities “are reimbursed timely for the full amount of the difference between their acquisition cost for the selected drug and the MFP within 14 days.” Finally, CMS will also require a manufacturer “to submit its process for making the MFP available for the selected drug in writing to CMS at least 30 days before the start of the [IPAY].”

These methods and timelines are unnecessary and exceed CMS’s statutory authority. Section 1193 instructs CMS to “determine (and, by not later than the last date of such period, agree to) a maximum fair price for such selected drug of the manufacturer in order for the manufacturer to provide access to such price” to MFP eligible individuals. Nowhere does the statute prescribe *how* manufacturers must provide access to the MFP. We therefore recommend that CMS require that manufacturers provide access to the MFP—not dictate the specific methods for doing so. If manufacturers fail to provide the MFP to eligible individuals, the statute calls for the imposition of civil monetary penalties. These penalties—equal to ten times the difference between the price made available to eligible individuals and the MFP per unit sold—are sufficient deterrents to prevent manufacturers from withholding the MFP. At a minimum, the proposed deadlines are impracticable and manufacturers should be provided at least 90 days to provide reimbursement.

There will be significant challenges associated with verifying the eligibility of patients who are dispensed selected drugs. Since only Medicare beneficiaries are MFP eligible individuals, manufacturers will need a process to verify that they, and only they, receive selected drugs at the MFP. This process is of even greater concern for 340B covered entities who typically provide the 340B ceiling price to any patient. Manufacturers will need to validate that 340B entities are only providing the MFP to eligible individuals. Allowing manufacturers flexibility to verify claims and provide access to the MFP to eligible individuals—particularly in the first few years of the program—would benefit all parties. Thus, CMS should not require particular methods or timelines for providing access to the MFP. Instead, CMS should adopt a collaborative posture and work together with manufacturers to deliver the MFP to eligible patients and dispensers.

5. CMS should reconsider which patents and exclusivities it intends to analyze and how these mechanisms will impact the MFP (section 60.3.4 and Appendix C).

CMS’s approach to considering pending and approved patent applications and exclusivities will stifle innovation and, in some cases, exceeds the Agency’s statutory authority. The Guidance states that “CMS intends to consider the length of the available patents and exclusivities before the selected drug may no longer be single source. For example, if the selected drug has patents

and exclusivities that will last for a number of years, CMS may consider adjusting the preliminary price downward.”²² Using the existence of patents and exclusivities to drive down the preliminary price is inconsistent with the purposes of these mechanisms, which are intended to incentivize and reward development of innovative medicines. In other words, the existence of these protections signals that the therapy is novel, which should counsel in favor of a higher, not lower, MFP. In addition, penalizing a product for remaining patents would deprive manufacturers of part of their value. Because patents are valuable property, and CMS appears to be intentionally considering reducing the value of that property by proposing an inverse relationship between MFP and remaining patent life, CMS’s action may constitute a taking requiring just compensation under the Fifth Amendment’s Takings Clause.²³ CMS should therefore commit not to lower the MFP of a drug due to remaining patent protections or exclusivities.

Moreover, although the statute directs CMS to consider “[d]ata on pending and approved patent applications . . . for the drug,” CMS suggests it will consider a broader swath of patents, e.g., using terminology such as “patents linked to the selected drug where the Primary Manufacturer is not listed as the assignee/applicant.”²⁴ This approach is inconsistent with the statute which, under the heading of “manufacturer-specific data” includes information on “pending and approved patent applications.”²⁵ By expanding its analysis of patents beyond the manufacturer, CMS exceeds its statutory authority. Accordingly, CMS should only examine patents specific to the manufacturer of the selected drug.

6. CMS should not use the price of therapeutic alternatives as the starting point for its initial offer analysis (section 60.3).

Elements of CMS’s method for developing an initial MFP offer are in tension with the text of the statute. Section 1194(b)(1) encourages CMS to “achieve the lowest maximum fair price for each selected drug.” To accomplish this goal, CMS must consider negotiation factors including “the extent to which such drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives.”²⁶ The cost of therapeutic alternatives is, therefore, intended to be a *factor* in the developing the MFP. Yet, CMS grants this one factor an outsized role in the Guidance by stating that the Agency will use Part D net price(s) and/or the Part B ASP of therapeutic alternatives “to determine a starting point for developing an initial offer.”²⁷

The cost of therapeutic alternatives is not a suitable starting point for developing MFP offers. First, this methodology does not comport with the structure of the statute. The statute requires CMS to consider two sets of factors—(1) manufacturer-specific data, and (2) evidence relating to alternative treatments. All enumerated factors should be considered together when setting the MFP. Here, however, CMS is giving one part of one factor—the cost of therapeutic alternatives—outsized influence. We acknowledge that CMS has committed to “adjusting the starting point

²² Guidance, at 53.

²³ U.S. Const. Amend. V; see *Horne v. Dept. of Agriculture*, 576 U.S. 350, 359-60 (2015).

²⁴ Guidance, at 88.

²⁵ SSA § 1194(e)(1).

²⁶ *Id.* § 1194(e)(2)(A).

²⁷ Guidance, at 47. If a therapeutic alternative is unavailable, CMS intends to base the initial offer on the Federal Supply Schedule or “Big Four Agency” Price. *Id.*

using the negotiation factors.”²⁸ Nevertheless, the statute requires CMS to consider all factors rather than overweighting one factor and merely “adjusting” the MFP based on an analysis of the others.

Furthermore, such a method does not account for the unique clinical attributes that an individual product might have. Rather than considering each product’s risks and benefits, it bluntly collapses them into categories. It also fails to consider the unique pricing strategies of different products. For example, a recently launched product may provide steep rebates to gain market share in its first few years on the market. Starting the initial offer analysis from this arbitrarily low price would not be a true reflection of the cost of alternatives during the period the selected drug is subject to the MFP.

Instead of using the price of therapeutic alternatives as the default starting point, CMS should develop its initial offer based on the statutorily mandated MFP ceiling. From that point, CMS can conduct a holistic examination of all the relevant negotiation factors that preserves the public health and rewards novel innovations.

7. CMS should adopt a more expansive definition of research and development (R&D) costs (section 60.3.4 and Appendix C).

CMS should consider a wide variety of manufacturer-specific data during the negotiation process. As noted, section 1194(e)(1) requires CMS to consider factors including “[R&D] costs of the manufacturer for the drug and the extent to which the manufacturer has recouped [R&D] costs.” To calculate R&D costs, CMS intends to “compare the [R&D] costs and the global, net revenue reported by the Primary Manufacturer.”²⁹ In Appendix C of the Guidance, CMS explains that it will examine all costs “incurred by the Primary Manufacturer for all FDA-approved indications of a drug.”³⁰ Other R&D costs, such as certain trials, are also limited to those conducted specifically for FDA approval.

Comparing R&D costs directly attributable to FDA-approved indications with global revenue is imprecise, and unduly prejudicial to manufacturers, because it results in an apples-to-oranges comparison. For example, global revenue may take into account indications or presentations of an active ingredient that are not approved by FDA and were supported by separate (including regional) clinical studies. These revenues would “count” under CMS’s approach, whereas the R&D costs needed to generate the supportive data would not, because the relevant approval would not be from FDA. This calculation of R&D costs thus is inaccurate and would always prejudice the manufacturers. CMS should instead adopt a methodology that compares R&D costs and revenues on an appropriate, apples-to-apples basis.

In addition, CMS’s definition of R&D costs for abandoned or failed products is overly restrictive. According to the Guidance, CMS will only consider R&D costs for abandoned and failed products “with the same active moiety / active ingredient or mechanism of action as the selected drug that did not make it to clinical trials.”³¹ This method of accounting for R&D costs does not comport with pharmaceutical industry standards. Rather than looking at costs across active moieties or active ingredients, investments are typically calculated for the particular disease

²⁸ *Id.*

²⁹ Guidance, at 52.

³⁰ *Id.* at 82.

³¹ *Id.* at 84.

state. We therefore encourage CMS to broaden the scope of failed or abandoned drug costs to include all investments in the relevant disease state.

At minimum, if CMS refuses to expand its definition of R&D, the Agency should clearly note its method of calculation in all publications related to specific selected drugs. In particular, CMS should clearly define the various inputs examined in its published explanation for the MFP. In the Guidance, CMS notes that these published explanations may contain “high-level comments about the data submitted to CMS, without sharing any proprietary information,” such as saying that the “manufacturer has recouped its R&D costs.”³² Since CMS’s definition of R&D differs from the industry standard, particularly with respect to calculating abandoned or failed products, we urge CMS to dispel any confusion by publicly stating its definitions of key concepts and noting they may differ from other established ways of calculating R&D recoupment.

8. Monitoring of bona fide marketing after a product has exited the Program is unnecessary (section 90).

CMS’s plan to monitor the bona fide marketing of generics and biosimilars *after* the Agency has determined that such competition exists exceeds statutory authority, and this Guidance content should be deleted. In section 90.4, CMS states that it “intends to monitor whether robust and meaningful competition exists in the market *once it makes such a determination* [that a generic or biosimilar has been approved and marketed].”³³ To carry out this goal, CMS explains that it may examine the availability of the product in the “pharmaceutical supply chain” or the “share of generic drug or biosimilar biological product units identified in Part D PDE data.”³⁴

The purpose of this continued monitoring is unclear. The text of the statute clarifies that a product “shall be referred to as a ‘selected drug’ with respect to such year and each subsequent year beginning before the first year that begins at least 9 months after the date on which the Secretary determines at least one drug or biological product . . . is approved or licensed . . . [and] in marketed pursuant to such approval or licensure.”³⁵ The “determination” that a generic or biosimilar is “approved or licensed” and “marketed pursuant to such approval or licensure” is made at a particular time point, not on a continuous basis. If a generic or biosimilar meets those criteria, the innovator product is removed from the selected drug list. The statute does not contemplate a claw back procedure or continual reassessment of whether the exit criteria are met. Accordingly, CMS’s decision to monitor compliance is puzzling. Given the statute’s provision that the determination is binary, further monitoring beyond the determination serves little purpose. To the extent CMS implies that it can re-list a drug that has been removed, on the basis that “bona fide marketing” has ceased, the statute does not contain any authority for such action. Accordingly, this monitoring serves no practical purpose.

Beyond the evident problems associated with CMS purporting to play the role of a competition authority, such monitoring is both excessive and unauthorized. BI therefore recommends that CMS abandon any plans to monitor the ongoing marketing of generics or biosimilars.

³² *Id.* at 85.

³³ *Id.* (emphasis added).

³⁴ *Id.* at 67-68.

³⁵ SSA § 1192(c)(1).

9. CMS must ensure that selected drugs are not disfavored by Part D plan sponsors (section 110).

As written, section 110 creates perverse incentives for Part D plan sponsors that could undermine the very purpose of the Program. Currently, the Guidance requires that Part D formularies “include each covered Part D drug that is a selected drug . . . during the Contract Year (CY) 2026 and all subsequent years for which the MFP of the selected drug is in effect.”³⁶ This requirement does not go far enough.

Mere inclusion is insufficient to ensure that CMS and Medicare beneficiaries reap the full rewards of the MFP. Certain Part D products that may be selected by CMS for the first round of negotiation treat tens of millions of Medicare beneficiaries with chronic conditions such as heart disease and diabetes. If CMS only requires inclusion of selected drugs on Part D drug plans, plan sponsors would have free rein to disfavor selected drugs by placing them on less favorable formulary tiers or through burdensome utilization management that goes beyond normal safety requirements. As a result, patients may find that out-of-pocket costs for their prescriptions have increased. Despite receiving clinical benefit from and having familiarity with their current medications, some patients may be forced to change products. Many Medicare patients may take multiple products subjected to negotiation which would compound the disruption.

CMS would also be negatively affected by the unfavorable tiering of selected drugs. If Medicare beneficiaries switch to alternative treatments, CMS would be deprived of the savings the IRA was designed to capture. In addition, allowing Part D plans to disfavor selected drugs may complicate the negotiation process, because manufacturers will be unaware of the kinds of rebates they will be able to provide to plan sponsors.

To remedy this problem, CMS should require that Part D plans not penalize selected drugs compared to non-selected drugs in the same therapeutic class. In other words, Part D plan sponsors should be required to provide selected drugs parity with similar non-selected drugs. Parity can be achieved if CMS requires that Part D plans cover selected drugs (1) on the most favorable formulary tier afforded any brand name product in the therapeutic class and (2) without overly burdensome utilization management.

10. The Guidance Fails to Mitigate Constitutional Defects in the IRA and Raises New Constitutional Concerns.

Sections 1101 and 1102 of the IRA raise serious constitutional concerns that are not mitigated (and in some instances are compounded) in the Guidance. As an initial matter, as discussed above, the drug pricing provisions of the IRA raise issues under the Takings Clause of the Fifth Amendment.³⁷ The Supreme Court has recognized that patents are property protected by the Fifth Amendment³⁸ and that government regulation can constitute a taking when it substantially reduces the value of the private property.³⁹ Where the Guidance goes beyond what the statute requires—such as by compelling Secondary Manufacturers to provide Primary Manufacturers with proprietary information—it compounds these takings concerns.

³⁶ Guidance, at 70.

³⁷ U.S. Const. Amend. V.

³⁸ See *Horne v. Dept. of Agriculture*, 576 U.S. 350, 359-60 (2015).

³⁹ See, e.g., *Pennsylvania Coal Co. v. Mahon*, 260 U.S. 393, 415 (1922).

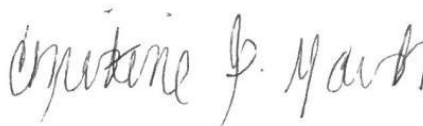
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Boehringer Ingelheim appreciates the opportunity to provide feedback on these proposals and looks forward to working with CMS to inform the development of meaningful policy solutions. Thank you for considering these comments and those submitted by PhRMA. If you require any additional information or have questions, please contact Michael Penn, Head of Public Policy at (203)791-6680 or michael.penn@boehringer-ingelheim.com.

Sincerely,



Bridget Walsh
Vice President
Government Affairs & Public Policy
Boehringer Ingelheim Pharmaceuticals, Inc.



Christine Marsh
Senior Vice President
Market Access
Boehringer Ingelheim Pharmaceuticals, Inc.



April 13, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator, Centers for Medicare & Medicaid Services (CMS)
Department of Health and Human Services,
Hubert H. Humphrey Building, Room 445-G
200 Independence Avenue, SW
Washington DC 20201

IRARebateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Boundless Bio, Inc. appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance) (collectively referred to herein as, the Negotiation Program).

Boundless Bio is a private biotechnology company founded in 2018 out of innovations in cancer research deepening the understanding of unique cellular structures called extra-chromosomal DNA, or ecDNA, and the role ecDNA plays in driving some of the most aggressive and difficult to treat cancers, oncogene amplified cancers. Like many other diseases, the aging population served by Medicare is also hugely impacted by cancers driven by oncogene amplification. Boundless Bio is committed to applying its deep understanding of ecDNA biology to deliver transformative therapies to these patients.

At Boundless Bio, we are just celebrating the news that our first investigative new drug application (IND) was accepted by the US Food and Drug Administration (FDA) and we are able to bring forward our first ecDNA directed investigational drug (ecDTx) in a human clinical trial



this year; however this excitement is also dampened by our concern that we will be unable to raise enough capital to successfully bring this drug, and other ecDTx in our pipeline, through the development process. The implementation of Section 30.1 of the Negotiation Program will apply government price controls to small molecule drugs like ours within 9 years of launch (v. 13 for biologics), which will disincentivize investments in small molecule programs like ours in favor of biologics.

We recognize that CMS has stated that its guidance on Section 30 is final and it is not seeking or accepting comments on this Section. We are highly concerned by this action given the significance of the topics included in Section 30. Respectfully recognizing that CMS is *not* permitting comments on Section 30, we submit our comments here in the context of what we *would have submitted* had comments on Section 30 been permitted.

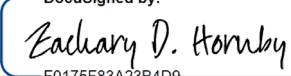
Essentially, it is a very simple story. We are working on the cutting edge of cancer science in a new area of biology, ecDNA, to develop safe and effective medicines to treat very aggressive types of cancer in patients who do not have other effective treatment options and are consigned to an extremely poor survival prognosis. Our ecDTx are orally administered small molecules, which bring many benefits to patients who may be treated at home with a pill and avoid the stress of traveling to outpatient centers and the added cost and discomfort of undergoing infusion procedures to receive their medicine. If our ecDTx drugs, solely due to their status as small molecules, are to be given four years less time on the market than biologics before negotiated prices are applied, Boundless Bio may be unable to continue to attract enough funding to complete development. Research and development funding dollars will be diverted to biologics, which the new rules now afford a greater period of time for market-based pricing. We expect that funding to enable important scientific advances in small molecule cancer treatment, like ours, will simply dry up.

We respectfully request that government price controls for small molecules begin at 13 years, the same time at which government price controls are applied to large molecules. This will remove incentives that will skew research and development funding away from important small molecule drug development innovations, like ours, and allow treatments for patients to be brought forward without arbitrary bias toward large molecules.



We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact us by e-mail at legal@boundlessbio.com or by telephone at (858) 766-9912 if you have any questions regarding our comments.

Regards,

DocuSigned by:

F0476F83A23B4D9...
Zachary D. Hornby

VIA ELECTRONIC DELIVERY to: IRAREbateandNegotiation@cms.hhs.gov

April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator, Director of the Center for Medicare
Centers for Medicare & Medicaid Services
200 Independence Avenue SW
Washington, DC 20201

Re: Medicare Drug Price Negotiation Program Guidance

Dear Dr. Seshamani,

Bristol Myers Squibb (BMS) appreciates the opportunity to comment on the Centers for Medicare & Medicaid Services (CMS) *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026* (“Guidance”).¹

At BMS, we are inspired by a single vision—transforming patients’ lives through science. We are in the business of breakthroughs—the kind that transform patients’ lives through lifesaving, innovative medicines. Our talented employees come to work every day dedicated to the mission of discovering, developing, and delivering innovative medicines that help patients prevail over serious diseases. We combine the agility of a biotech with the reach and resources of an established pharmaceutical company to create a global leading biopharma company. In oncology, hematology, immunology, and cardiovascular disease—with one of the most diverse and promising pipelines in the industry—we focus on innovations that drive meaningful change.

BMS supports Medicare policies that promote beneficiary access to new and effective medical treatments and help ensure Medicare patients benefit from the innovation that defines the U.S. health care system. That is why we do not support the Medicare “negotiation” and price setting policies contained in the *Inflation Reduction Act (IRA)*. We are extremely concerned by the impact that these policies will have on clinical research and future innovation for patients. BMS believes that, in the absence of full repeal of the IRA’s drug pricing provisions, significant clarity and reforms are necessary in several critical areas.

It is essential for CMS to promote and allow for full transparency and input on IRA implementation. BMS opposes the Agency’s purported “final” Guidance on product scope and selection, in substance and process. As explained below, CMS’ approach in this matter is disappointing, inappropriate, and unlawful, as CMS is using the Guidance to impose new

¹ CMS, “Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments” (March 15, 2023), available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

substantive requirements on manufacturers and otherwise go beyond the statute and constitutional requirements. The Agency must seek public input on a matter of such public impact and importance, and where private rights are at stake. There is also an overriding constitutional requirement for robust and meaningful engagement on CMS' proposals regarding fundamental issues that have been apparent since the IRA's enactment in August 2022.

BMS appreciates the opportunity to provide the following comments on the Guidance. We intend our input to help CMS improve transparency and clarity of the IRA's price setting program. Our recommendations reflect and are driven by our deep expertise in pharmaceutical innovation, and we offer them to help mitigate against the unintended and negative consequences the Guidance would have on innovation and, most importantly, patients.

Key comments include:

- **Product Scope and Selection:** BMS disagrees with CMS' decision to issue Section 30, Identification of Selected Drugs for Initial Price Applicability Year 2026, as "final." CMS has yet to make any determinations of qualifying single source drugs (QSSDs), which will occur with the first published QSSD selections. In the Guidance, however, CMS is seeking to redefine what qualifies as a QSSD in a way that disregards statutory commands. The Guidance also seeks to impose new substantive obligations without undertaking notice-and-comment rulemaking required by due process. Even beyond those critical legal concerns, given the importance of product scope for eventual selection and price setting, as well as the downstream negative implications to innovation and patient access for years beyond 2026, we urge CMS to meaningfully consider, and respond to, stakeholder feedback on these important topics. (*Section 30*)
- **Price Setting Methodology:**
 - Negotiation Factors and Data Elements: BMS is pleased that CMS is proposing to consider an array of evidence submitted by manufacturers on the selected drug, as well as pertinent evidence submitted by the public on therapeutic alternatives. However, we are deeply concerned by the stringent evidence submission limits and the lack of transparency regarding CMS' process for considering comparative effectiveness evidence and other manufacturer data to inform a Maximum Fair Price (MFP). We appreciate the opportunity to comment on and reiterate the importance of considering a broad perspective when conducting value assessments and urge the Agency to place an emphasis on patient-centric benefits when setting the price. (*Sections 50, 60, and Appendix C*)
 - Establishment of a Single MFP: BMS understands CMS' desire to convert utilization across a medication's dosage forms and strengths into a consistent 30-day equivalent supply. BMS believes the methodology that CMS has proposed, with adequate adjustment to ensure alignment with statutory language, could accomplish the necessary goal of establishing a single MFP. In any event, BMS strongly urges CMS to consult manufacturers of selected drugs on the methodology to be used for determining the MFP for a selected drug. (*Section 60.1*)
 - MFP Calculation: BMS is concerned that the descriptions of the MFP calculations lack sufficient clarity and introduce certain ambiguities that may make it challenging for manufacturers to follow the methodology and accurately replicate calculations for selected products. Notably, CMS proposes to apply the MFP ceiling twice: a first time at the drug level, and a second time at the dosage form or strength level. CMS should not—and, indeed, may not under the statute, as explained below—finalize this proposal. (*Sections 60.2 & 60.5*)
 - MFP Offer Amount: BMS is concerned that CMS' proposed process by which the Agency will determine an offer will de-value pharmaceutical advancements that are currently on the market and result in even greater chilling effects on future innovation. To preserve patient access to lifesaving and quality enhancing medicines, BMS urges CMS to carefully consider situations where a selected drug should be paid fairly at the maximum price. (*Section 60.2*)

- Developing an Initial Offer: BMS strongly objects to the use of the Federal Supply Schedule (FSS) or Big 4 price as a reference point for the initial offer. By also referring to final FSS and Big 4 prices, CMS would be capturing complexities of those calculations that should not apply to IRA price setting. Reference to FSS and Big 4 prices could have the unintended consequence of reducing or eliminating manufacturers' voluntary discounts that lead to lower prices for those government channels. Further, such pricing may be inherently short-term and thus would serve as an inappropriate benchmark for setting a longer-term price. *(Section 60.3.2)*
- **Negotiation Process**: BMS believes that it is essential for CMS to develop and finalize a process for determination of an MFP that is open and transparent, so that stakeholders can reasonably predict how the determination of an MFP will operate in practice. We note that it is *especially* important that CMS be fully transparent regarding the negotiation and renegotiation methodology and process. BMS appreciates CMS sharing initial high-level thoughts in the Guidance, but we believe that additional details are needed, with an opportunity for stakeholders to have full visibility into the methodology and process, as well as the opportunity to provide comment on such forthcoming details to better inform the parameters. *(Section 60)*
 - Initial Offer and Justification: It is critical for manufacturers to have a full understanding of the context and basis for the MFP offer. To increase transparency and further CMS' two-way dialogue with a manufacturer of a selected drug, we urge the Agency to consider releasing a confidential report to the manufacturer alone, alongside the initial offer and justification, to better inform manufacturer counteroffers and subsequent data submissions. *(Sections 60.3 & 60.4)*
 - Negotiation Process After Counteroffer: BMS has serious concerns with CMS' process for interfacing with manufacturers of selected drugs. While we agree with CMS that meetings after any rejection of a manufacturer's counteroffer are necessary and will allow for a more efficient and effective process, initiating meetings with manufacturers only after such rejection is too late. There must be meaningful engagement throughout CMS' process. In our vast experience with negotiating with states and payers, the proposed process would be highly unusual and arbitrary, and would not even approximate a proper negotiation—which, for instance, does not feature limitation on engagement between parties, in contrast with CMS' contemplated limitation to three meetings. *(Section 60.4.3)*
 - Confidentiality: BMS agrees with CMS that the Agency should ensure that confidential commercial information submitted by manufacturers during the negotiation process is protected from disclosure. We believe it is imperative that CMS ensure adequate safeguards to protect manufacturers' trade secret, proprietary, and other confidential commercial information from disclosure, including the opportunity for manufacturers to receive notice of potential disclosure and the opportunity to object to such disclosure. BMS also asks CMS to carefully consider how the Agency intends to keep confidential commercial information confidential within the Agency itself. *(Section 40.2.1)*
- **Effectuating Access to the MFP**: BMS supports efforts to lower patient out-of-pocket costs and appreciates the complexity of providing discounts to Medicare patients at the point-of-sale. To help mitigate operationalization issues, BMS strongly asserts that additional data safeguards are necessary, regardless of the MFP discount effectuation option, to ensure a transparent and administratively efficient operationalization of MFP access (inclusive of ensuring that appropriate patients are gaining access to the MFP). It is critical for stakeholders, including CMS, to have the right information at the right time to ensure compliance. This is especially essential given the lack of a dispute resolution process set forth in the Guidance. *(Section 40.2.2)*
 - 340B Non-Duplication: BMS appreciates the opportunity to comment on 340B non-duplication. CMS needs to provide clarity on how the Agency intends to operationalize this non-duplication provision of the IRA, as the Guidance does not provide adequate specificity to effectuate this provision. *(Section 40.4.1)*

- Diversion and “Spillover”: The statute requires that the MFP the government sets should be accessible to ***MFP-eligible beneficiaries only***. BMS is highly concerned with diversion and appropriation of the MFP beyond the intended Medicare market (*i.e.*, “spillover”) and supports efforts by the Agency to help ensure that the MFP goes only to the beneficiaries for whom the MFP is calculated and intended.
- **Other Considerations:**
 - Transparency and Record Preservation: BMS opposes CMS’ proposals to restrain manufacturer speech in relation to information acquired during the price setting process, including the Agency’s proposal to mandate destruction of manufacturer property under certain circumstances. The proposals violate the First Amendment and run contrary to principles of fairness, transparency, and accountability. (*Section 40.2.2*)
 - Civil Monetary Penalties (CMPs): Especially given the unparalleled magnitude of contemplated CMPs in the novel IRA framework, BMS advocates for CMS to implement strong, special safeguards to protect against erroneous and inappropriate CMP application. Among other things, CMS should provide notice of any perceived deficiency that could result in CMPs and provide at least 30 days to cure any such deficiency. CMS should offer the opportunity for manufacturers to dispute CMS’ findings prior to imposition of CMPs.
 - Dispute Resolution Process: BMS is disappointed that the Guidance does not appear to contemplate a dispute resolution process. BMS strongly believes that the statute’s limitation on administrative and judicial review does not prohibit CMS from establishing a dispute resolution process, and furthermore, there is strong policy and operational rationale for doing so.
 - Part D Formulary Access: While BMS agrees with CMS that Part D formularies must cover a selected drug for which an MFP is in effect, we note that it is critical for health plans to design formularies in ways that promote beneficiary access to all medicines, both MFP and non-MFP medicines. We are disappointed that CMS did not propose additional beneficiary safeguards, in light of longstanding issues of beneficiary access related to certain practices by plans and pharmacy benefit managers (PBMs), and we ask CMS to convey to plans the necessary expectation that they do not engage in measures to disadvantage selected drugs. (*Section 110*)

BMS also generally supports the comments written by the Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Innovation Organization (BIO), though we present our BMS-specific views below.

Section 10 – Introduction

BMS disagrees with CMS’ decision to issue Section 30 as “final,” without solicitation of, and opportunity for, public comment. We appreciate the complexity and operationalization that CMS must undertake prior to implementing the goals of the IRA. But anticipated operational challenges do not preclude opportunity and need for public input on critical and fundamental aspects of IRA implementation. The Agency must carefully consider key matters of product scope and selection to help alleviate patient access risks related to the nation’s most relied-upon medicines. Matters such as how to identify a distinct “product” under the statutory framework have been apparent for over half a year. The Agency could have long sought public input on product scope and selection, either in a previously released guidance or in this Guidance. And the Agency should have done so, rather than promulgating as “final” far-reaching Guidance that imposes new substantive obligations, does not reflect the statutory framework, and risks causing a host of concerns—above all, raising further barriers to Medicare beneficiary access to innovative medicines.

The IRA will have vast ramifications for patients, providers, manufacturers, and other stakeholders across the country. BMS is concerned that misinformed, misguided, or unlawful implementation could have sweeping negative

repercussions with respect to Medicare beneficiary access to needed medicines, and, indeed, for *all* patients. It is vital for CMS to make every effort to maximize transparency and fairness, including meaningful consideration of and response to stakeholder feedback on its proposals, and staying within the bounds of statutory and constitutional requirements.

We therefore urge CMS to solicit and consider fully all stakeholder feedback on Section 30 for the initial price applicability year (IPAY) and future years, despite the policies contained in that section being stated in the Guidance as “final.” Further, we urge CMS to continue engaging the public on these critical issues, including through a distinct round of notice-and-comment rulemaking following this Guidance, given the deprivation of comment opportunity and the lengthy amount of time before product selections are published half a year from now.

CMS notes that “this [G]uidance is not subject to the notice-and-comment requirement of the Administrative Procedure Act or the Medicare statute... [and] that notice and public procedure on this [G]uidance would be impracticable, unnecessary, and contrary to the public interest....”² BMS questions CMS’ conclusion as to notice-and-comment requirements, and otherwise strongly disagrees that notice-and-comment is impracticable, unnecessary, and contrary to the public interest. Public input on matters of such public importance is inherently in the public interest—while avoiding public input, as the Agency seems to be doing in its “final” Guidance, is contrary to the public interest, and also compromises private rights that are at stake. Especially given its novel proposals on product scope and selection (many of which conflict with statutory language and practical considerations), stakeholder input is necessary, and the need for it is compelling. It is inappropriate for CMS *not* to seek public feedback on this process, and such omission runs counter to the Agency’s previous statement that it intends to “prioritize transparency and robust engagement among all interested parties”³ in implementing the statute.

As CMS knows, “[t]he purpose of [a] comment period is to allow interested members of the public to communicate information, concerns, and criticisms to the [A]gency.”⁴ Equally important is the Agency’s timely explanation of how such information, concerns, and criticisms factored into its final decision-making. This is what allows the comment process to serve its intended role of facilitating a “genuine interchange” of ideas between the Agency and interested members of the public.⁵ The process of responding to discrete points raised by commenters helps to ensure that the Agency is carefully considering the feedback it received from the public—“the interchange of ideas between the government and its citizenry provides a broader base for intelligent decision-making and promotes greater responsiveness to the needs of the people.”⁶ Further, when an Agency is not interpreting a statute, but instead seeking to impose substantive obligations beyond what the plain text requires, backed by the specter of massive penalties, it cannot rely on guidance or interpretive rules, which are otherwise meant to be non-binding. The imposition of binding legal obligations must instead go through processes designed to allow for public input and ensure accountability.

We ask CMS, in finalizing any proposals, to include its responses to comments received and meaningfully explain the rationale for its decision-making. Naturally, because CMS indicated at present that it is not accepting comments on Section 30, the Agency cannot consider any feedback on Section 30 provided by stakeholders at this stage to represent the full public input it could have solicited, as CMS’ directive inherently has dissuaded stakeholders from voicing their full opinions on these matters, if they venture to voice any opinions at all.

² Guidance at 2.

³ CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026 (Jan. 11, 2023), *available here* <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf>.

⁴ *Conn. Light & Power Co. v. NRC*, 673 F.2d 525, 530 (D.C. Cir. 1982).

⁵ *Id.*

⁶ *Buschmann v. Schweiker*, 676 F.2d 352, 357 (9th Cir. 1982) (internal quotation marks and citations omitted).

In short, the matters falling under Section 30 deserve a genuine interchange of ideas between the public and the government, and CMS should reissue Section 30 and open the Guidance therein for comment. If CMS were to open Section 30 for public input, for instance, BMS and other stakeholders would be in the position to provide comment on critical issues related to IRA implementation, including but not limited to:

Total Part D Expenditures:

- CMS confirms an interpretation of gross covered prescription drug costs that, in our view, would comport with the statutory meaning of the term.

Identifying Qualifying Single Source Drugs

- CMS states that it will identify “qualifying single source drugs” (QSSDs) at the active moiety/active ingredient level. That approach, however, is contrary to and beyond the scope of the IRA statute, creates unnecessary confusion in the face of statutory clarity, departs from well-established means of identifying products, and will be detrimental to future innovation and patient access to crucial medicines.
- Clear statutory commands may not be disregarded. The statute makes no mention of active moiety or active ingredient and establishes plainly that each single source product must have at least seven or 11 years elapsed after approval to be eligible for selection. The “earliest” approval language in the Guidance has no basis in the statute, but comes from whole cloth, and undermines incentives for innovation in a way not conceived by Congress. The statutory text specifies that a QSSD is defined by reference to each “such approval” or “such licensure” that starts each seven- or 11-year clock. It therefore requires that a distinct QSSD be defined by reference to a distinct approval or licensure. This plain reading of the statute is the beginning and end of the analysis.
- If CMS were to open its policy for public comment, it could consider detailed information on a prudent alternative approach that would be consistent with the statute and that would also provide certainty on key components. For example, an approach that may come from engagement with stakeholders could result in CMS identifying QSSDs by reference to a distinct New Drug Application (NDA) or biologics license application (BLA); aggregating expenditures across dosage forms and strengths within each distinct NDA or BLA; and applying MFP across dosage forms and strengths specific to each such NDA or BLA.
- Such an alternative approach would have many benefits that could be detailed in public comment, including:
 - consistency with the Food and Drug Administration (FDA) approval framework for NDAs and BLAs, a well-settled regulatory landscape that Congress showed no indication of departing from and indeed cross-referenced in the IRA, and which reflects FDA’s established understanding, contrary to CMS’ approach in the Guidance, that certain fundamental changes—not only in active ingredient or moiety—warrant thorough regulatory evaluation of the product as distinct from an already-existing one;
 - consistency with the statutory term “covered Part D drug,” defined by reference to the statutory term “covered outpatient drug” under Section 1927(k)(2) of the Social Security Act, where products are distinguished by NDA approval and BLA licensure;
 - consistency with the IRA statute’s balance between the often-competing interests in encouraging pharmaceutical and biotechnology innovation and reducing prescription drug prices, reflected by, among other things, the establishment of a time period post-NDA approval or post-BLA licensure during which selection for price setting is unavailable; and
 - establishment of a bright-line test for all parties under the price setting process, allowing ready identification of distinct products by CMS and permitting manufacturers to confidently track the seven- or 11-year timeline from the initial NDA/BLA approval date for selection eligibility and make research and development decisions accordingly.

- Ultimately, though, what remains clear is that the Guidance takes an approach that Congress did not intend, and the Agency should solicit public comment to ensure that it does not disregard statutory commands and otherwise risk constitutional concerns.

Determining Generic/Biosimilar Competition

- BMS has serious concerns with CMS' policy to consider a generic drug or biosimilar product to be "marketed" when the Prescription Drug Event (PDE) data substantiates that "the manufacturer of that drug or product has engaged in bona fide marketing of that drug or product." Those serious concerns are doubled by CMS' suggestion that it will continue to "monitor" marketplace sales to evaluate whether there is "robust and meaningful competition" from a generic or biosimilar, in determining whether a selected drug remains ineligible for price setting. "Bona fide marketing" and "robust and meaningful competition" are not phrases or concepts included in the statute, and CMS' attempt to create such standards is *ultra vires*.
- Had this matter been opened for public comment, BMS and other stakeholders could have explained how this policy is contrary to the plain language of the IRA statute, *e.g.*:
 - Under the statute, a selected single source product can no longer be defined as "selected drug" after the Secretary's determination that at least one generic drug or biosimilar has been approved or licensed, as applicable, and "is marketed pursuant to such approval or licensure." Although Congress gave the Secretary responsibility for the *determination* that such approval or licensure and marketing has occurred, the statute's plain words establish the objects of that determination.
 - At a threshold level, price setting applies only to a *single source* product, meaning that if a *different* source exists (*i.e.*, a generic or biosimilar), the product categorically cannot come from a single source. Further, the plain meaning of the statutorily unqualified term "marketed" reveals that Congress did not contemplate extra-statutory concepts related to degree of utilization or "robust and meaningful" competition.
 - Both CMS and FDA have long determined a product to have been marketed based on a point-in-time standard. For instance, CMS has long used this concept in the Medicaid Drug Rebate Program (MDRP), where "market date" has been defined in guidance to mean "the earliest date the drug was first marketed under the application number of any labeler,"⁷ and where "marketed" is defined under the National Drug Rebate Agreement to mean the date on which the product was first "available for sale by a manufacturer in the states."⁸ Congress would have understood this common-sense, established approach in drafting the IRA provisions.
- Interposing subjective, indefinite criteria in the determination of when a generic is "marketed" is inappropriate, subject to abuse, *ultra vires*, and inconsistent with the terms of the statute. It also risks introducing a number of practical complexities and drawbacks, including unnecessary lag with respect to termination of MFP and concomitant adverse effects on generic/biosimilar competition, contrary to what Congress has sought to promote.
- BMS therefore supports CMS taking a position that aligns with the "market date" reported under the MDRP because it presents an established, uniform standard that would help ensure that manufacturers are not inappropriately subject to selection, negotiation, application of an MFP, or an excise tax. Adopting this standard would also help ensure clarity and consistency in the identification of these key dates under Medicare price setting. BMS urges CMS to use this standard for identifying both: (1) the date on which a generic or biosimilar is first marketed; and (2) the date on which CMS determines that to be the case (which, ideally, should be the same as the actual marketing date to prevent complexities involving potential inappropriate delay in removal from "negotiation" or MFP applicability).

⁷ CMS, MDRP Data Guide § 5.15 (Apr. 2022).

⁸ National Drug Rebate Agreement § I(l), 83 Fed. Reg. 12,770 (Mar. 23, 2018).

Orphan Drugs

- CMS should take care not to implement price setting in any way that could risk undermining the patient-centric incentives at the core of the Orphan Drug Act (ODA). In the last 40 years, the ODA framework has supported the development, approval, and distribution of products that meet pressing, often unmet, public health needs, and otherwise might not ever be available.
- If CMS were to accept comment on Section 30, BMS and other stakeholders could provide detailed input relevant to application of the orphan drug exclusion. For instance, CMS should be aware that consulting relevant databases noted in the Guidance is ultimately insufficient. The databases may not always reflect the fact that a drug indication is within the scope of the orphan drug designation, in which case CMS should allow manufacturers to provide evidence that it does so. CMS should also consider other statutorily consistent practices, such as looking at orphan designation at the time of selection (and not looking to any previous designation that has been withdrawn) and promoting orphan drug development by clarifying that the seven- or 11-year clock for identifying QSSD status of an orphan drug starts on the date an orphan drug loses its status as an excluded orphan drug.

Plasma-Derived Products

- CMS has announced a two-step approach for identifying excluded plasma-derived products: (1) referring to product information on FDA's Approved Blood Products website, and (2) referring to FDA's Online Label Repository to verify if the product is derived from human whole blood or plasma, with FDA consultation "as needed."⁹
- Had CMS solicited comment on this practice, BMS and other stakeholders could have identified flaws in this approach and emphasized that the statutory exclusion of plasma-derived products should be applied based on the facts and circumstances of each product, applying the words of the statute itself. Instead, CMS has purportedly finalized an approach that risks sweeping into the IRA framework a statutorily excluded plasma-derived product.
- CMS should apply the statutory plasma-derived products exclusion to encompass all products falling under this provision. Further, the possibility that some products may not be captured in the two-step approach CMS has envisioned here underscores the need for CMS to provide advance notice of potential selection of a product for "negotiation," should this or any other statutory exclusion apply.

Product Selection

- CMS has purportedly finalized the process for selection of drugs for IPAY 2026. Had the Agency sought comment on this part of the Guidance, BMS and other stakeholders could have provided full comment on important related considerations. For instance, CMS should bear in mind that while the Agency has discretion to determine which particular drugs are selected, Congress has not delegated discretion to redefine what drugs qualify for selection.
- Hence, there is an inherent risk that, without appropriate engagement with manufacturers, CMS could engage in *ultra vires* selection of a drug, such as publishing a drug statutorily ineligible for selection, or take action that raises constitutional concerns related to equal protection given to the selection of particular drugs for particular manufacturers. The Agency could mitigate against such risks by engaging with stakeholders to confirm that its approach comports with the statute and the discretion granted to the Agency under the statute. Further, the Agency should provide advance notice to applicable manufacturers of drugs *anticipated* for selection and offer those manufacturers the opportunity to raise concerns before ultimate selection.

⁹ Guidance at 11.

- To help ensure lawful and appropriate selection, the Agency could also consider, among other measures: (1) providing at least one quarter of such advance notice to manufacturers of drugs anticipated for selection; (2) providing the same such advance notice to the manufacturers of the next five drugs (should drugs anticipated for selection be determined ineligible); and (3) providing biosimilar manufacturers the opportunity to inquire as to whether a particular reference biologic is among the drugs anticipated for selection. If advance notice conflicts with CMS' final determination of delay for certain biologics, CMS could explain in such advance notice that a delay request has been submitted and is being actively considered.

Biosimilar Special Delay Requests

- CMS has purportedly finalized substantial guidance related to the biosimilar manufacturer special delay request process. Had CMS solicited comment, BMS and other stakeholders could have offered many relevant suggestions and ideas for consideration to inform Agency policy.
- For instance, CMS refers to the statutory unavailability of a delay request where an agreement exists between a biologic manufacturer and a biosimilar manufacturer that imposes "improper constraints"¹⁰ on the biosimilar manufacturer but does not identify the contours of such an agreement that would give rise to such improper constraints in the view of the Agency. Consistent with the statute, the Agency should determine an agreement is disqualifying *only* when the agreement explicitly requires submission of an initial delay request. As the Agency recognizes, certain agreements could inform whether "high likelihood" exists of biosimilar entry in a specified period. Presuming "improper constraints" in an agreement, rather than looking to the language of the contract itself, risks nullifying the statute's contemplation of these other agreements informing "high likelihood" determinations.
- Relatedly, BMS and other stakeholders could provide valuable insight on the "high likelihood" determination itself. If comment were open, we would encourage CMS to reasonably make such a determination based on the best available information and consider further information that could help inform whether high likelihood exists (e.g., FDA's views of data and information submitted in the BLA, FDA communications about BLA status, the biosimilar manufacturer's production and distribution arrangements and progress, and information the biosimilar manufacturer concludes to be relevant to the determination). The statute permits the Agency to consider such other information and could also permit a biosimilar manufacturer supplementation through a timely request based on recent information or otherwise for good cause.
- BMS and other stakeholders could also provide insight on the biosimilar delay process, including the submission deadline. Setting a deadline as close as reasonably possible to selection would help ensure the best available information for consideration of the request, whereas the date established without stakeholder input creates a very tight timeframe that could result in critical information not being considered. The Agency could also notify the reference biologic manufacturer of a request and delay selection and price while the Agency evaluates all information submitted, and also provide notice of determination in advance of the selected drug publication date, allowing the biosimilar manufacturer to bring any error or other concern to CMS' attention before such date.

As of now, however, we understand from the Guidance that CMS is not accepting any comment on Section 30. We therefore hope that CMS will consider our points above and limited examples for the narrow yet important purpose of reissuing Section 30 with an opportunity for full public input on these and other critical matters.

¹⁰ *Id.* at 19.

Section 40 – Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026

CMS notes that the Agency intends to sign an Agreement with the Primary Manufacturer of each selected drug and does not intend to enter into an Agreement with any Secondary Manufacturer(s) of a selected drug. CMS also indicates that the Primary Manufacturer is responsible for collecting and reporting the Secondary Manufacturer's information as well as ensuring that the Secondary Manufacturer(s) make(s) the MFP available to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers.

BMS does not agree with this approach, which is found nowhere in the statute and, at the very least, could not be imposed without proper rulemaking procedures. It is also impractical. "Primary Manufacturers" have no ability to attest to, nor would it be appropriate for them to opine on, the data of another manufacturer or ensure that other manufacturers are making the MFP available to the respective parties. CMS has elsewhere understood "the challenges of obtaining pricing information from unrelated manufacturers," including "concerns about data sharing with competitors," which has the potential to raise antitrust concerns.¹¹ CMS should recognize the same concerns in this context and should ensure that undue liability is not placed on Primary Manufacturers to report information that is practically and legally unavailable to them.

40.1 Entrance into an Agreement with CMS

CMS notes that it will "make reasonable efforts to make the final text of the Agreement available to the public before the selected drug list for [IPAY] 2026 is published."¹² BMS contends that CMS must allow manufacturers to review the "Agreement," with all proposed terms, well in advance of the drug selection date. Otherwise, manufacturers will see such terms for the first time when they must execute the Agreement. The specific terms greatly matter, given the private rights at stake and the prospect of enormous CMPs associated with violations of such terms. Manufacturers also need lead time to establish or modify compliance systems or protocols, so that they can be prepared to be in compliance when they execute the Agreement.

BMS believes the Agreement into which a manufacturer must enter should include certain key components and safeguards and align strictly with statutory requirements. BMS agrees with the flexibility CMS intends to give to a manufacturer in providing access to the MFP for eligible individuals, including through a rebate, and the document's plain terms should establish that flexibility. As further discussed in our comments to Section 40.4 of the Guidance, the Agency should also commit to ensuring providers report a "minimally necessary"¹³ data set to the manufacturer or its vendor to be entitled to access the MFP and for validating their right to access in a timely manner, according to standard business practices and consistent with non-duplication requirements. The Agency should also set forth sufficient and robust provisions to ensure the protection of a manufacturer's confidential and proprietary information, as the statute requires. Finally, with respect to penalty provisions, the Agency should provide for pre-sanction dispute resolution and the opportunity to cure and/or dispute before any penalty may be imposed or publicly disclosed.

Manufacturers must submit to CMS all names, titles, and contact information for representatives authorized to execute the Agreement and conduct the negotiation just five days after CMS publishes the list of selected drugs. If CMS publishes the selected drug list, as directed, on September 1, 2023, that would be the Friday prior to the Labor Day holiday. We are concerned that it might be difficult to reach the Agency during this critical time should we have a product selected

¹¹ 81 Fed. Reg. 5,169, 5,266, 5,271 (Feb. 1, 2016).

¹² Guidance at 27.

¹³ HHS, "Does the Privacy Rule permit health plans to disclose protected health information to pharmaceutical manufacturers for the adjudication of drug rebate contracts?" (June 2003), available at <https://www.hhs.gov/hipaa/for-professionals/faq/455/does-hipaa-permit-health-plans-to-disclose-information-to-pharmaceutical-manufacturers/index.html>.

and need assistance with said Agreement. We therefore seek clarification that CMS intends to have staff available over the Labor Day holiday to assist with issues pertaining to this task. CMS has also indicated that one of the persons must be legally authorized to bind the Primary Manufacturer to the terms and conditions contained in the Agreement and access the CMS Health Plan Management System (HPMS) to sign the agreement; we would appreciate CMS' clarification in advance as to which employee(s) would be legally authorized and recommend against a C-suite representative. BMS also asks that CMS update manufacturers on the approximate timing for when HPMS will be updated with the respective changes needed to facilitate the Agreement and data elements.

40.2.1 Confidentiality of Proprietary Information

BMS agrees with CMS that the Agency should ensure that confidential commercial information submitted by manufacturers during the negotiation process is protected from disclosure, as any inappropriate disclosure or use of manufacturer sensitive business information would raise considerable Fifth Amendment takings concerns. It is imperative that CMS ensure adequate safeguards to protect manufacturers' trade secrets, proprietary, and other confidential commercial information from disclosure. In addition, we urge CMS to afford manufacturers the ability to proactively identify information as proprietary for the Agency's consideration, as well as allow manufacturers the ability to review any public facing documents related to the MFP prior to sharing publicly.

BMS also asks CMS to carefully consider how the Agency intends to keep confidential commercial information confidential within CMS. We have related concerns over CMS' potential use of the information as a market participant, as opposed to strict use for the purposes of IRA "negotiation" and price controls, and insufficient protections against disclosure of information as part of the public MFP explanation, given the private rights at stake for the manufacturer. CMS must implement additional procedures to ensure confidentiality, including the following.

Determination of Confidential Commercial Information: BMS thanks CMS for proposing to adopt a familiar standard to protect proprietary and confidential information. Notably, under Exemption 4 of FOIA, a manufacturer may designate submitted information as trade secret, proprietary, or otherwise confidential, and CMS may not disclose such information without providing adequate notice to the manufacturer of its intent to do so and a reasonable opportunity for the manufacturer to object.¹⁴ In the Guidance, CMS does not contemplate an opportunity for manufacturers to designate submitted information as trade secret, proprietary, or otherwise confidential and/or how the Agency will provide adequate notice for disclosure of information. If CMS were to allow such an opportunity for manufacturers, however, there would be an opportunity for the Agency to have a greater understanding of which data are public or not. For example, under FDA's regulations, the existence and status of a pending application, in addition to information contained in a pending NDA or BLA, generally are protected from public disclosure.¹⁵ Only once a decision on an application is final will some, but not all, information regarding the application be subject to disclosure. We ask CMS to clarify these safeguards and urge the Agency to provide the maximum amount of transparency and flexibility. If nothing else, we ask CMS to consider ensuring confidentiality standards consistent not only with what is required under FOIA, but also under government drug price reporting programs, like the MDRP.

¹⁴ See 45 C.F.R. §§ 5.41, 5.42.

¹⁵ See 21 C.F.R. §§ 314.430(b) ("FDA will not publicly disclose the existence of an application...before an approval letter...or tentative approval letter is sent to the applicant..., unless the existence of the application...has been previously publicly disclosed or acknowledged."); id. § 314.430(c) ("If the existence of an unapproved application or abbreviated application [for a small molecule drug] has not been publicly disclosed or acknowledged, no data or information in the application or abbreviated application is available for public disclosure."); id. § 601.51(b) ("The existence of a biological product file will not be disclosed by [FDA] before a biologics license application has been approved unless it has previously been publicly disclosed or acknowledged."), id. § 601.51(c) ("If the existence of a biological product file has not been publicly disclosed or acknowledged, no data or information in the biological product file is available for public disclosure."); see also 39 Fed. Reg. 44,602, 44,634 (Dec. 24, 1974) ("The existence of a pending NDA constitutes confidential commercial information where the existence of clinical testing has not previously been publicly disclosed or acknowledged.").

Stringent Storage and Access Requirements: CMS should also confirm that all trade secret, proprietary, and other confidential commercial information will be stored in a secure manner, accessible only by CMS staff who have a program-based need to access such information, and accessible only when needed for work involving the program. CMS already implements such protections with product and pricing data submitted by manufacturers participating in the MDRP. For example, under the MDRP, data is uploaded to an online interface that both states and manufacturers access. Functionality of the interface, however, is limited by the user's role: state users do not have the ability to view quarterly or monthly pricing records or all product information because "some of this information is confidential (*e.g.*, Baseline Average Manufacturer Price (AMP) data)."¹⁶ This important level of protection will minimize the risk of inadvertent disclosure of highly confidential data submitted by manufacturers and encourage greater transparency between CMS and manufacturers. Thus, CMS should adopt and specify safeguards with respect to storage and the platform through which program information will be submitted.

Confidentiality Safeguards with Respect to the Public Explanation of the MFP: BMS notes that it benefits all parties—including CMS—if the Agency openly discloses the informational assumptions that it relies upon in developing offers and responses. By disclosing the informational bases of such offers and responses, CMS will facilitate a more open and transparent dialogue during the negotiation process. For example, manufacturers will be able to better understand CMS' positions and rationales and thereby tailor more appropriate counteroffers and replies. Furthermore, open disclosure of the non-manufacturer-submitted information upon which CMS relies will reduce the risk of CMS' offers and responses being viewed as a misunderstanding or misinterpretation of such information—because manufacturers will be in a position to raise any such errors or misapprehensions to the Agency's attention.

While supportive of transparency in MFP offers and counteroffers, BMS is concerned about the potential for improper disclosure of confidential commercial information when CMS publishes the statutorily-required explanation of the MFP for a selected drug.¹⁷ Given that the MFP will likely be based at least in part on drug pricing and other confidential commercial information, it is critical that CMS prevent disclosure of such information as part of this explanation, including through redaction or omission of data. In fact, the statute explicitly requires such protection of confidential information with respect to the MFP explanation, by cross-reference to the general duty of confidentiality identified above.¹⁸ We ask that CMS expressly confirm that, in publishing the explanation for the MFP, it will ensure that trade-secret, proprietary, and other confidential commercial information will not be directly or indirectly disclosed.

Furthermore, BMS believes that a manufacturer should be permitted to identify for CMS any way in which the intended explanation of the MFP would reveal confidential commercial information. To help ensure that such information will not be inadvertently disclosed, we ask CMS to afford the manufacturer a reasonable opportunity to review and raise confidentiality concerns regarding CMS' intended explanation of the MFP, in advance of its publication.

40.2.2 Data Use Provisions and Limitations

BMS joins PhRMA in its comments with respect to this section of the Guidance. We oppose CMS' proposals to restrain manufacturer speech in relation to information acquired during the negotiation process. We also oppose the proposal to mandate destruction of manufacturer property (*i.e.*, the "destruction of data"). Among other things, these unprecedented proposals violate the First Amendment and run contrary to principles of fairness, transparency, and accountability. The proposals should be withdrawn, and CMS should engage stakeholders regarding appropriate and lawful measures to impose in connection with data use.

¹⁶ CMS, Medicaid Drug Programs (MDP) User Manual 1 (Nov. 3, 2021).

¹⁷ SSA § 1195(a)(2).

¹⁸ *Id.*

40.4 Providing Access to the MFP

BMS supports efforts to lower patient out-of-pocket costs and appreciates the complexity of providing discounts to Medicare patients at the point-of-sale. BMS is pleased that CMS is proposing to allow manufacturers to have flexibility to provide access to the MFP through an up-front discount or retrospective reimbursement (herein referred to as “a rebate”), and we appreciate the opportunity to comment on this topic. However, to help ensure a transparent and administratively efficient operationalization of the MFP, BMS strongly asserts that additional data safeguards are necessary, regardless of the MFP discount effectuation option. It is critical for stakeholders, including CMS, to have the right information at the right time to ensure compliance. This is especially essential given the lack of a dispute resolution process.

Concerns with Diversion: Under the law, manufacturers must provide access to the MFP for a selected drug to:

1. Maximum fair price eligible individuals “enrolled in a prescription drug plan under [Medicare] part D... or [a Medicare Advantage (MA)-prescription drug (PD)] plan under [Medicare] part C... if coverage is provided under such plan for such selected drug” or to “the pharmacy, mail order service, or other dispenser” with respect to such individuals, and
2. “[H]ospitals, physicians, and other providers of services and suppliers with respect to maximum fair price eligible individuals” who are “enrolled under [Medicare] part B... , including an individual who is enrolled in an MA plan under [Medicare] part C... , if payment may be made under part B for such selected drug.”¹⁹

Units of a selected drug purchased at the MFP, therefore, may only be dispensed to MFP-eligible individuals. Despite this clear statutory limitation, the Guidance does not explain how CMS will help prevent providers and pharmacies from administering or dispensing MFP-purchased units of selected drugs to MFP-*ineligible* individuals. Absent clear indications of how CMS intends to help uphold the statutory requirements, manufacturers must have flexibility to provide access to MFP-eligible individuals only as required, without risk of CMPs.

Necessity for System Changes, and Challenges with Supporting MFP Effectuation and Mitigating Diversion: Both discount mechanisms that CMS acknowledges (chargebacks and rebates), as they operate today, fall short of the operational capability to enable manufacturers to accurately provide access to the MFP. To adapt either mechanism to provide access to the MFP, significant enhancements or a redesign must occur, which will require time and coordination among stakeholders—particularly those that do not work together currently. CMS should make clear that it expects providers to submit MFP validation data, which will encourage the types of system changes necessary to support the smooth adoption of MFP.

- **Chargeback System Challenges:** Chargebacks support discounts when a dispensing outlet is eligible to purchase at a single, validated, up-front discounted price for all patients. The U.S. chargeback system is based upon saleable packages, but the MFP is extended based upon an eligible patient, provider, and claim. The current chargeback data set is thus inadequate to support the MFP validation. Specifically, new connections to different stakeholders would need to be built to capture additional fields such as payer information, prescription level data, etc. These types of significant changes may face stakeholder pushback within the given timeframe unless CMS establishes this MFP validation data expectation as a requirement.
- **Rebate System Challenges:** Rebates in the U.S. are customarily paid after validation of claims data, which makes the rebate mechanism appropriate for extending a discount that depends on patient-level information (such as the MFP). However, adjustments to existing rebate data elements and how dispensers

¹⁹ SSA §§ 1191(b)(2), 1193(a)(3).

would be paid the rebate would need to occur to accommodate the MFP. Additional data elements would need to be added to the existing rebate system to ensure alignment with the nonduplication provision, which is discussed in our response to section 40.4.1.

Concerns with Unclear Timing Expectations: BMS is concerned with the lack of clarity in CMS’ statement that it “intends to require that a Primary Manufacturer ensure that pharmacies, mail order services, and other dispensers as well as intermediate entities, such as wholesalers, as applicable, are reimbursed timely for the full amount of the difference between their acquisition cost for the selected drug and the MFP within 14 days.”²⁰ This sentence has unclear meaning. For example, “within 14 days” could refer to a multitude of events, each of which with significant meaning for manufacturers (*e.g.*, within 14 days of the dispensing date may be too short of an interval, and therefore operationally infeasible, especially given the 340B complications addressed in Section 40.4.1). And, as noted below, this imposition of timing, however construed, is otherwise unrealistic.

Recommended CMS Actions: CMS should make clear that providers seeking to benefit from the MFP must report a minimally necessary data set to the manufacturer or its vendor for the purposes of MFP discount validation in a timely manner, according to standard business practices, and in alignment with non-duplication requirements. CMS should expressly acknowledge that manufacturers may establish, receive, review, and, as necessary, audit MFP validation data to ensure MFP access in accordance with the statute. Additionally, CMS cannot expect manufacturers to provide access to the MFP and respond “to CMS requests within specified timeframes with documentation demonstrating compliance”²¹ unless the manufacturer has the necessary MFP validation data, in the timeframe needed, to demonstrate its compliance. Access to and use of this validation data is also pivotal to CMS’ enforcement of the statute, which we address further in section 90.2.

Specifically, it is BMS’ strong belief that CMS should clarify and lengthen the 14-day timeframe, given the new processes that need to be developed to make this work and the 340B complexity. The Agency could instead clarify that timeframes for data submission and validation will be determined by the manufacturer, in conjunction with and with input from stakeholders, and shared with CMS in December 2025 as outlined in the Guidance.

BMS urges CMS to further clarify its intention to define “providing access to the MFP” as ensuring that the amount paid by the dispensing entity for the selected drug is no greater than the MFP. If a provider disregards the standard business practices associated with the MFP validation data (*e.g.*, does not submit the data, submits incomplete data, submits data outside of the timeframe, etc.), the amount paid by the dispensing entity for the selected drug might be greater than the MFP, but through no fault of the manufacturer. To address that circumstance, CMS should clarify that providers have a responsibility to follow standard business practices when requesting the MFP.

Although it may be helpful for CMS to solicit feedback on a standard, mandatory MFP validation data set, a claims clearinghouse, and a process by which manufacturers may receive PDE data, it would be understandably challenging for CMS to arbitrate such data elements given the variety of products and different manufacturer business approaches. CMS should instead affirm that providers are expected to submit MFP validation data and then provide flexibility for manufacturers to establish the appropriate data set and process, given the individual product and channel. This approach should achieve a result that could be more easily adjusted over time than a solely CMS-directed mechanism and would relieve the Agency from complex administrative responsibilities. CMS should also acknowledge that the MFP validation data elements, if submitted pursuant to health care operations purposes, would not need to be de-identified for HIPAA purposes. Taking that step would provide better transparency than if providers were required to rely on third

²⁰ Guidance at 32.

²¹ *Id.* at 26.

party vendors to deidentify data, and it would likely result in quicker resolution of potential disputes among stakeholders. Each manufacturer would notify CMS in writing by December 2, 2025, of the method the manufacturer intends to use to provide access to the MFP.

CMS should clarify its statement that manufacturers or their contracted entities shall not charge any transaction fee for “this process.”²² BMS agrees that patients should not be charged a transaction fee; however, transactional fees among intermediaries are standard practice (*e.g.*, switch fees, administrative fees, etc.). Because the MFP effectuation mechanism is not yet determined, it is premature for CMS to disallow standard business practice fees among intermediaries. If CMS interferes with intermediary fees, it may introduce contractual complexity or could disincentivize intermediaries from prioritizing or offering Medicare services, disrupting the effectuation process. It is also unclear that CMS has the authority to regulate fee-charging among private parties through this Guidance, or at all.

While BMS appreciates CMS confirming that it intends to provide flexibility in the discount mechanism, BMS urges CMS to make clear that providers seeking to benefit from the MFP must report a minimally necessary data set to the manufacturer or its vendor for the purposes of MFP discount validation in a timely manner, according to standard business practices, and in alignment with non-duplication requirements. CMS should expressly acknowledge that manufacturers may establish, receive, review, and as necessary, audit MFP validation data to ensure manufacturers have provided MFP access in accordance with the statute.

40.4.1 Nonduplication with 340B Ceiling Price

BMS appreciates the opportunity to comment on 340B non-duplication, as, by statute, a manufacturer of a selected drug cannot be required to offer both the MFP and the 340B price on the same unit.²³ BMS is seeking specific clarity from CMS on how the Agency intends to operationalize this non-duplication provision of the IRA, as the Guidance does not provide adequate specificity to effectuate this provision. BMS agrees with Secretary of Health and Human Services (HHS) Xavier Becerra’s comments during a recent House Energy & Commerce Health Subcommittee hearing on the HHS Fiscal Year 2024 Budget Request, when the Secretary stated that the 340B program does not have the transparency the program needs to be successful, and that compliance and transparency are two critical reform areas.²⁴ In this section, we provide suggestions for CMS to take steps aligned with Secretary Becerra’s comments. Clarity from CMS is essential on this topic, as the responsibility of the manufacturer to provide access to the MFP depends upon the 340B status of the patient and provider in some circumstances, and adequate transparency is also essential for CMS to oversee and enforce compliance.

Size/Scope of the MFP-340B Overlap: The Medicare-340B overlap is significant—according to a new all-market analysis by IQVIA, for example, the estimated 340B overlap in Part D is 40.1% and in Part B is 36.3%, meaning that \$34.0B to \$37.5B of sales may be at risk for MFP-340B duplicate discounts.²⁵ This is a sizeable problem that CMS cannot ignore, especially given the statutory non-duplication mandate.

Root Cause of MFP-340B Complexity: Chargebacks and Replenishment: As a root cause issue, 340B is extended via a chargeback model. That is demonstrably problematic because chargebacks are used to extend discounts at the provider/outlet level based on saleable package sizes, but 340B discount eligibility depends on the provider, patient, and

²² *Id.* at 32.

²³ SSA § 1193(d).

²⁴ See House Energy & Commerce Committee Health Subcommittee Hearing, “Fiscal Year 2024 Department of Health and Human Services Budget” (March 29, 2023), available at <https://energycommerce.house.gov/events/health-subcommittee-hearing-fiscal-year-2024-department-of-health-and-human-services-budget>.

²⁵ IQVIA, “Can 340B Modifiers Avoid Duplicate Discounts in the IRA?” (February 21, 2023), available at <https://www.iqvia.com/locations/united-states/library/white-papers/can-340b-modifiers-avoid-duplicate-discounts-in-the-ira>.

covered outpatient drug status (in practice, on a claims basis). This mismatch has contributed to the complex and extra-statutory 340B replenishment model that attempts to compile and connect the 340B eligibility (claims) information and reconcile it to the 340B purchasing (chargeback) information, but it has faced challenges and resulted in program integrity concerns.^{26,27} Because the requirement for a manufacturer to provide access to the MFP is conditional on the Medicare-coverage status of the patient, 340B-patient eligibility status, and 340B and MFP prices of a drug, 340B transparency must be addressed.

How MFP Validation and Provision Is Tied to 340B: There are two key points of connection between the decision to extend the MFP discount and the 340B program:

- **Calculating the MFP discount amount to reimburse a provider is currently tied by CMS to actual acquisition cost (AAC), and AAC is tied to 340B in some situations.** CMS is proposing to require a manufacturer to reimburse the provider “the full amount of the difference between *their acquisition cost for the selected drug* and the MFP within 14 days,”²⁸ but the complicated 340B replenishment/chargeback model obscures the fundamental data point needed for a manufacturer to accomplish this task: the *acquisition cost*. The manufacturer would be left to compute a mathematical equation to extend the MFP, but the key variable (AAC) is missing. In the 340B replenishment/chargeback model, the inventory identity, and thus the corresponding AAC, is transformed from 340B to wholesale acquisition cost (WAC) and from WAC to 340B in a non-transparent manner after a claim has been dispensed. Further complicating this situation, not all patients of a 340B entity are 340B eligible, so a manufacturer cannot assume that if 340B is lower than the MFP, that it should extend 340B automatically. The National Council for Prescription Drug Programs (NCPDP) describes this issue in its Reference Guide:
 - “In many cases it is impossible at the point of a claim submission to know that Section 340B drugs will be used and therefore pharmacies would be *unable to submit the 340B acquisition cost*.”²⁹
 - “The processes used by a covered entity to determine whether Section 340B drugs will be used *are prerequisites to any exchange of information* concerning section 340B drugs, and if applicable, *associated pricing*.”³⁰
- **The current open-ended timeframe for 340B determination is like a swinging gate—which will drag CMS, manufacturers, and providers back and forth through it—disrupting the non-duplication provision and ultimately resulting in disorderly MFP extension and CMS enforcement.** Adding further complexity, the timeframe for these non-transparent inventory/AAC status decision changes from WAC to 340B and from 340B to WAC, as NCPDP states, “varies greatly... and can be as brief as same day or as long as never... [or] as long as infinity.” That will prevent CMS from policing abuses, because the MFP access decision is tied to a 340B decision

²⁶ See, e.g., GAO, “Drug Discount Program: Federal Oversight of Compliance at 340B Contract Pharmacies Needs Improvement” (2018), available at <https://www.gao.gov/assets/gao-18-480.pdf>; see also PHSA § 340B(a)(5)(A).

²⁷ See, e.g., Examining HRSA’s Oversight of the 340B Drug Pricing Program: Hearings Before the Subcomm. on Oversight & Investigations of the H. Comm. on Energy & Commerce, 115th Cong. 2–3 (2017) (noting limited oversight against diversion and that between 63 and 82 percent of audited 340B covered entities have been found to be noncompliant with at least one program requirement) (statement of Rep. Tim Murphy), available at <https://www.congress.gov/115/chrg/CHRG-115hhrg26929/CHRG-115hhrg26929.pdf>; T. Okon, *Hospitals and for-profit PBMs are diverting billions in 340B savings from patients in need*, Stat News, <https://www.statnews.com/2022/07/07/for-profit-pbms-diverting-billions-340b-savings/> (June 7, 2022); see also PHSA § 340B(a)(5)(B).

²⁸ Guidance at 32 (emphasis added).

²⁹ NCPDP, “340B Information Exchange Reference Guidance Version 2.0” (June 2019), available at https://ncdpd.org/NCPDP/media/pdf/340B_Information_Exchange_Reference_Guide.pdf. Emphasis added.

³⁰ *Id.*

that changes according to the entity's own timeframe and "requirements for determining patient eligibility to use Section 340B drugs."³¹

Recommended CMS Actions: BMS recommends that CMS take the same action needed to support the MFP access provision: CMS should make clear that providers seeking to benefit from the MFP must report a minimally necessary data set to the manufacturer or its vendor for the purposes of MFP discount validation in a timely manner, according to standard business practices, and in alignment with non-duplication requirements. CMS should expressly acknowledge that manufacturers may establish, receive, review, and as necessary, audit MFP validation data to ensure manufacturers have provided MFP access in accordance with the statute. Without this CMS support, the statute cannot be faithfully implemented, and manufacturers will be left in an impossible position of not knowing how to comply with the statutory requirements, all while under the threat of penalty for perceived non-compliance.

CMS Precedent for MFP Validation Data Submission: CMS has already recognized the importance of claims data in publications regarding Medicaid and 340B, and these recommendations are also germane for Medicare. We agree with CMS' specific statements and suggest CMS apply its own guidance for the MFP: "When states provide claims level data to manufacturers, we would expect there to be a reduction in number of disputes due to more accurate information being provided.... Manufacturers likely need claims level data for true invoice validation purposes... [and] If claims level data is provided, this may reduce the state's administrative burden and expense of researching manufacturer dispute issues."³² Additionally, the statute clearly states that manufacturers must provide access to the MFP based upon MFP-eligible individuals, and data would support that provision.

CMS Should Support Transparent Data Provision: How MFP validation data is supplied is a critical component to support marketplace transparency. In the 340B landscape, "black box" approaches have been attempted—where there is reliance on a vendor to take deidentified data sets and match them in a black box. These models are not transparent, and they are complicated and difficult to audit. Incomplete data inputs lead to incomplete outcomes, and voluntary processes that allow partial data submissions or rely on inaccurate input data ultimately do not provide the needed transparency. Importantly, the minimally necessary data set that could be used for MFP discount validation falls under the health care operations exception under HIPAA, so de-identification would not be required. CMS should acknowledge that addressing these transparency challenges in a manner that ensures visibility of the MFP validation data is critical to successful MFP operationalization. It would also be helpful for CMS to clarify that a final 340B eligibility determination at the point-of-sale aligns with CMS' 340B modifier mandates, which would help resolve the MFP-340B complexity.

In summary, it is not necessary for CMS to solve the 340B non-duplication complexity itself by creating datasets or business rules. CMS should and need only make clear that providers seeking to benefit from the MFP must timely report a minimally necessary data set to the manufacturer or its vendor for the purposes of MFP discount validation according to standard business practices, and in alignment with non-duplication requirements. CMS should expressly acknowledge that manufacturers may establish, receive, review, and as necessary, audit MFP validation data to ensure manufacturers have provided MFP access in accordance with the statute. If CMS does not require this, providing access to the MFP in the non-duplicated manner required becomes infinitely challenging, if not impossible.

Section 50 – Negotiation Factors

BMS is pleased that CMS is proposing to consider an array of evidence submitted by manufacturers and the public on the selected drug and therapeutic alternatives as part of its effort to "negotiate" MFPs. However, we are deeply

³¹ *Id.*

³² CMS, "Best Practices for Avoiding 340B Duplicate Discounts in Medicaid" (Jan. 2020), *available at* https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/cib010820_107.pdf.

concerned by the stringent evidence submission limits as outlined in the Guidance, as well as the Negotiation Data Elements Information Collection Request (ICR), including the lack of transparency regarding CMS' process for considering comparative effectiveness evidence and other manufacturer data to inform an initial MFP.

BMS urges CMS to finalize a consistent, standardized format for the submission of manufacturer-specific data, with the flexibility to permit reasonable assumptions and submit additional data to account for the distinctive qualities of the treatment selected for negotiation. While we understand that CMS will be undertaking a significant exercise in reviewing data submitted by manufacturers and other stakeholders on comparative effectiveness information, we are concerned that the text data format and rigid word limits proposed will constrain the ability of manufacturers to share important evidence on the values of our medications. When submitting a dossier to the Agency, there should neither be limitations on file sizes nor transmission options.

CMS must acknowledge that it is impossible to capture the full value of a treatment in a “one-size-fits-all” approach to data submissions and must provide manufacturers the ability to submit additional relevant data. Attempting to shoehorn countless varying technologies, business practices, and circumstances into a single framework without necessary context would inevitably result in less useful and incomplete information being considered by CMS.

BMS asks CMS to reconsider its proposal in order to ensure that any information collection process allows manufacturers to submit a comprehensive evidence package in the Academy of Managed Care Pharmacy (AMCP) dossier format, which is a widely used dossier submission format. In BMS' view, the AMCP dossier is the gold standard in both requiring and receiving clinical information from manufacturers for value assessment purposes. In addition, most manufacturers and payers have experience using the AMCP dossier format, which furthers feasibility, consistency, and transparency in the value assessment process.

In addition, we recognize that this value assessment process will be a significant, and novel, undertaking for CMS. It is for this reason that BMS believes that broad stakeholder input is critical to ensuring that value assessments are robust, accurate, and transparent—not the least of which being manufacturer input. As the entity responsible for developing the treatment from the discovery phase all the way to post market surveillance and beyond—a process that can span 20+ years—manufacturers have unique insight, data, and perspective about the health, economic, and societal impact that is critical to the value story of that treatment. On an annual basis, for example, BMS conducts over 500 studies (in addition to developing clinical trials). We strongly support an open dialogue between manufacturers and CMS during the value assessment process.

50.1 Manufacturer-Specific Data

BMS urges CMS also to specify that the Agency will consider any information submitted by manufacturers, even if that information is not tied to a specific statutory factor. This approach is consistent with the plain language of the statute. Like CMS “offers,” manufacturer “counteroffers” must be justifiable based on the statutorily enumerated factors. Nothing precludes manufacturers from voluntarily providing additional information to CMS that may also bear on the Agency's decision-making.³³ BMS notes that CMS has clear authority to consider all information submitted by manufacturers, whether or not tied to a statutory factor, and that the Agency should consider all information submitted by a variety of stakeholders. In addition, unlike justifications for offers or counteroffers, CMS' responses to counteroffers need not be justified by reference solely to the statutorily enumerated negotiation factors.³⁴ Please refer to BMS'

³³ See SSA § 1194(b)(2)(C)(ii)(II).

³⁴ Compare *id.* § 1194(b)(2)(B) and (C)(ii)(II) (justifications for offers and counteroffers must be based on statutorily enumerated negotiation factors), with *id.* § 1194(b)(2)(D) (no similar requirement for responses to counteroffers).

comments on Appendix C for further recommendations on manufacturer specific data submissions and PhRMA recommendations to limit required data on manufacturer specific factors to data already in the public domain.

50.2 Evidence About Therapeutic Alternatives for the Selected Drug

BMS is encouraged by the body of evidence that CMS intends to consider on the selected drug and alternative treatments, including, but not limited to, real world evidence (RWE), clinician expertise, and methodologically rigorous/scientifically sound studies. As selected drugs will be assessed in the middle of their lifecycle, there will be many complexities to consider with multiple indications and comparative effectiveness evidence that has accrued over time. We also note the challenges that lie ahead in developing a review process that captures the complete and long-term value of a treatment with full manufacturer buy-in and support. We appreciate the opportunity to comment on the data elements that will be used to complete the value assessment and **strongly assert that value assessments should include certain good practice principles that encourage a broad perspective of value.**

In a qualitative assessment, CMS has an opportunity to consider medication value broadly and holistically. This holistic consideration should go beyond rigid health care costs and health outcomes to consider the impact of medicines on society—such as improvements to patients’ and caregivers’ lives, efficiency and quality in the health care system, and equity across populations. Pricing and access decisions, like the proposed IRA price setting scheme, result in a share of the total benefit of a medication (the societal surplus) being distributed among the manufacturer, health care systems, and patients. **As CMS embarks on precedent-setting value assessments and pricing decisions, BMS believes explicit discussion around the share of the societal surplus with multiple stakeholders is critical to protect patient access to innovative treatment.**

CMS has indicated that it will conduct internal analytics as part of the evidence assessment process. BMS supports the use of indirect treatment comparisons, as these techniques compare the performance of treatment alternatives across trials or in real-world datasets, linking treatments via shared comparator arms. In addition, we encourage CMS to utilize techniques like match-adjustment to help address potential bias. BMS also supports the use of predictive modeling approaches that build on meta-analyses and indirect treatment comparisons, as modeling can synthesize data across clinical trials, real-world data, and priors to project future benefit for patients and health systems. BMS believes that a proper value assessment should be a collective process with manufacturer buy-in and support. To that end, should CMS generate RWE and/or employ modeling techniques, **BMS reiterates that it is critical for manufacturers to have the opportunity, and ample time, to review and comment on the underlying assumptions and approaches to support a good-faith, transparent value assessment.**

CMS indicates that priority will be given to studies focusing on special populations (including individuals with qualifying disabilities, patients with End-Stage Renal Disease (ESRD), and Medicare-aged populations) over studies for which these populations were not the primary focus. While BMS agrees that benefits and risks to these special populations are critical to assess, the smaller sample sizes of related studies may not be sufficient to draw definitive conclusions. **We recommend that evidence from these studies be considered of equal priority to evidence from larger studies that are better powered to draw comparative effectiveness conclusions. We also encourage CMS to consider evidence in other subpopulations, including patients with comorbidities and different ethnicities, when data is available.**

Use of Discriminatory Metrics in Value Assessment: BMS is encouraged that CMS has proposed to not consider quality-adjusted life years (QALYs) in comparative effectiveness research when used in association with life extension to avoid treating the life of an individual who is elderly, disabled, or terminally ill as lower value than another younger, non-disabled, and terminally ill individual. However, we are concerned that when submitting evidence, stakeholders may continue to submit reports that use cost effectiveness analysis with QALY, as CMS suggests its willingness to consider

select evidence from reports with QALY metrics. **We ask CMS to provide greater clarity to stakeholders in this area. In particular, we request CMS to specify that stakeholders must redact any and all references to cost per QALY analysis in ICR text submissions** to reduce the likelihood that CMS assessors could be exposed to such metrics, hopefully reducing the risk of biasing their qualitative decisions. In addition, as noted elsewhere, BMS strongly supports the ability for manufacturers to validate CMS' evidence evaluations, which would provide further safeguards against discriminatory metrics being used to assess and determine value of important medicines.

CMS has also solicited comments on other metrics, in addition to QALYs, that may treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. **BMS is concerned that use of alternative cost effectiveness analysis (CEA) methods like cost per Equal Value Life Year Gained (evLYG), a metric anchored to the QALY paradigm, could also effectively disadvantage these special populations as they would involve value-for-money comparisons to arbitrary thresholds.** Simply put, most methodological and ethical limitations of the QALY (*e.g.*, health equity, measurement of health states, non-health effects, severity etc.) still apply to the evLYG with the exception of Ageism and Disability discrimination.³⁵ In the UK, the National Institute for Health and Care Excellence (NICE) has set a higher threshold for patients with a life expectancy of two years or less after “a groundswell of public opinion and some evidence that society places extra value on the weeks and months at the end of life for terminally ill patients.”³⁶ Current NICE thresholds are about twice as high for end-of-life treatments and 5-10x higher for very rare diseases.³⁷ In developing a process for value assessment in the U.S., it is important for CMS to recognize that experienced HTA markets (*e.g.*, Germany, France, UK, Canada) with long established frameworks extend greater flexibilities related to value assessments, such as indication-specific assessments, unlimited word count on manufacturer dossiers, and transparency in the decision-making process. As it stands, CMS' proposal does not demonstrate fluidity in these areas where other markets, with longstanding value assessment experience, do offer these cooperative procedural elements. While new methods like generalized CEA are being explored to account for differential value of health improvement in different contexts, there is no consensus yet on the ability of these methods to adequately address health equity considerations for special populations. Further, CMS has not sought public comment from patients and other stakeholders on willingness to pay and appropriate cost effectiveness thresholds for IRA value assessments in general. **Therefore, BMS strongly recommends that CMS not anchor value assessments for selected drugs on CEA.** Any consideration of CEA should merely be a part of a broader and holistic assessment of value.

Stakeholder Input: Additionally, BMS supports CMS' proposal to consider evidence about therapeutic alternatives submitted by members of the public, particularly additional information that is not captured in the manufacturer's value dossier submission, with some modifications and safeguards. Active engagement with appropriate and relevant stakeholder groups throughout the value assessment process is very important. All relevant stakeholders (*e.g.*, patients, caregivers, health care professionals, regulators, and manufacturers) should have the opportunity to participate in the value assessment process, including the opportunity to comment on the methodology, the sources of evidence, and the draft assessment. **At minimum, CMS should seek feedback from patients, caregivers, and clinicians at key points through a formal meeting process (as the ICR process will not be sufficient to collect this type of feedback) to help ensure that the Agency selects appropriate therapeutic comparators, and understands benefits, unmet needs, and evidence to determine value. Additionally, stakeholders should be privy to the extent to which the Agency considered these value elements and how they impacted the MFP of a selected drug.** As the entity most familiar with a selected drug, BMS believes that manufacturers should be able to verify information submitted in relation to their product(s).

³⁵ Rand LZ, Kesselheim AS. Controversy Over Using Quality-Adjusted Life-Years In Cost-Effectiveness Analyses: A Systematic Literature Review. *Health Aff (Millwood)*. 2021 Sep;40(9):1402-1410. doi: 10.1377/hlthaff.2021.00343. PMID: 34495724.

³⁶ NICE, “NICE: 20 years of evidence-based decision making,” available at <https://indepth.nice.org.uk/20-years-of-NICE/index.html>.

³⁷ *Id.*

Section 60 – Negotiation Process

BMS believes that it is essential for CMS to develop and finalize a process for price setting that is open and transparent, so that stakeholders can reasonably predict how price setting will operate in practice. We note that it is especially important that CMS be fully transparent regarding the negotiation and renegotiation methodology and process. BMS appreciates CMS' sharing initial high-level thoughts in the Guidance document, but believes additional details are needed, with an opportunity for stakeholders to have full visibility into the methodology and process, as well as opportunity to provide comment to better inform the parameters. This visibility and opportunity for comment in advance of IPAY 2026, so that both manufacturers and CMS are adequately prepared going into the first round of price setting negotiations, is vital.

Congress specifically constructed the MFP setting process as a Drug Price *Negotiation* Program.³⁸ In doing so, Congress clearly intended there to be a process of meaningful engagement with opportunity for real dialogue.³⁹ Meaningful engagement and real dialogue can only occur through full transparency regarding stakeholders' comments and CMS' interpretation and evaluation of such comments. BMS urges CMS to commit to engaging in a process of meaningful engagement with opportunity for real dialogue, without arbitrary limitation on the scope of such dialogue (*e.g.*, through limitation of meetings). Not only is such commitment necessary to effectuate Congress's intent, but it will also promote greater transparency and information sharing. We also believe it will be readily manageable for the Agency, given the limited number of drugs subject to negotiation in any given year.

60.1 Establishment of a Single Proposed MFP for Negotiation Purposes

BMS understands CMS' desire to convert utilization across a medication's dosage forms and strengths into a consistent 30-day equivalent supply. While this methodology may yield a meaningful metric for certain Part D drugs which are exclusively in tablet form, taken at a consistent rate through the entire course of therapy, not approved for varying regimens to treat different indications, and not prescribed uniquely to each patient based on their own individual body weight or other personal characteristics, it is important for CMS to recognize that many products do not meet all of these criteria, which will preclude establishment of a single price that can be applied meaningfully to all national drug codes (NDCs).

Moreover, at a threshold level, CMS' calculation methodology takes an additional, unnecessary step that is contrary to the statutory requirement of the Agency to "establish[] procedures to compute and apply the [MFP] across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug."⁴⁰ Specifically, CMS proposes to apply the MFP ceiling twice—a first time at the drug level, and a second time at the dosage form or strength level. CMS should not—and, indeed, may not—finalize this proposal.

The statute defines both the MFP and the ceiling price as a price determined at the drug level. Nowhere does the statute contemplate the application of the ceiling price at the dosage form or strength level. The statute directs CMS to establish a process to apply the MFP—which already has been capped by the ceiling price—to each dosage form and strength of the selected drug, and it does not authorize the application of the ceiling price a second time. And as a factual matter, such double application could cause the MFP of some dosage forms and strengths of a selected drug to be reduced a second time. A WAC ratio for a dosage form or strength higher than 1.0 could generate a dosage

³⁸ See SSA § 1192(a)(3) (requiring CMS to engage in *negotiation*).

³⁹ See, *e.g.*, *Wheeler v. St. Joseph Hosp.*, 133 Cal. Rptr. 775, 790 (Ct. App. 1976) (distinguishing "negotiated contracts" from contracts of adhesion).

⁴⁰ SSA § 1196(a)(2).

form/strength-level MFP that is above the dosage form/strength-level ceiling price—and thus a dosage form/strength-level MFP that is doubly capped. This double capping would unfairly penalize dosage forms and strengths with a higher WAC ratio, even though such higher WAC ratio could merely reflect a difference in utilization, such as a difference in dosing regimen or a higher Part D utilization.

Beyond the threshold statutory issue with CMS' proposed calculation methodology, additional notable challenges with using a 30-day equivalent supply for pricing include:

- **Weight-based Dosing:** Many drugs (*e.g.*, certain IV drugs) have weight-based dosing that presents unique challenges to determining a 30-day equivalent supply. To apply this methodology, CMS would need to assume an average weight of the patients receiving weight-based dosing of a selected drug. There may be challenges with collecting data to accurately inform the average weight.
- **Dosing Variation Across Indications:** Some drugs have different dosing across indications, which also presents challenges to determining a single 30-day equivalent supply. For selected drugs that have different dosing across indications, CMS would need to determine the average 30-day supply for each indication, then calculate a weighted average based on relative use of the drug in each indication. There may be challenges with determining relative use across indications, especially if this changes over time. This also presents a significant complexity in an already convoluted approach.
- **Dosing Titration/Loading Doses/Changes in Dosing Over Course of Treatment:** Selected drugs with dosing titration, loading doses, or other changes in dosing throughout the course of treatment present challenges to determining a 30-day equivalent supply. CMS would need to develop a methodology for accommodating these changes in dosing.

The issues in calculating a 30-day equivalent supply mentioned above would also preclude meaningful comparisons to therapeutic equivalent products in many cases. For instance, many products are prescribed in combination with other drugs, which may be produced by other manufacturers. In this situation, comparisons of one manufacturer's drug to a single drug from another manufacturer would be further obscured, as neither reflects a complete course of therapy, and neither can simply be substituted for the other within that course of therapy.

In order for CMS to better understand and address the unique challenges in calculating a 30-day equivalent supply for a selected drug, CMS may want to consider adding questions to Appendix C regarding the drug's utilization (*e.g.*, approved regimens for each indication, loading doses and/or interruptions in dosing, titration over course of therapy, combination regimens, etc.). Given the significant limitations of the 30-day equivalent methodology, BMS also strongly urges CMS to consult manufacturers on the methodology to be used for a selected drug prior to the Initial Offer to better ensure any limitations are appropriately addressed and accounted for in the Initial Offer. With greater information, and in consultation with the manufacturer, CMS would be able to gain a better understanding of the drug's usage and determine how to make meaningful comparisons to therapeutic equivalents.

Recognizing that this 30-day equivalent methodology is new and unprecedented, we encourage CMS to consider alternatives where prior precedence exists, such as proposing prices at the NDC-11 level consistent with the FSS or at the NDC-9 level consistent with Medicaid.

In addition to the 30-day equivalent methodology, CMS also describes the steps for calculating the Ceiling for the MFP in Section 60.2.1, the Sum of Plan Specific Enrollment Amounts in Section 60.2.2, the Average Non-FAMP Price in Section 60.2.3, the Selection and Application of the Ceiling for the MFP in Section 60.2.4, and the Application of the MFP Across Dosage Forms and Strengths in Section 60.5. BMS is concerned that the descriptions of those calculations lack sufficient clarity and introduce certain ambiguities that may make it challenging for manufacturers to follow the methodology and

accurately replicate calculations for selected products. To provide greater clarity, we urge CMS to provide example calculations for illustrative drugs. These calculations should be representative of the complex situations described earlier, such as weight-based dosing or dosing variations across indications. The calculations will help ensure there is sufficient predictability in how CMS will interpret and apply these complex methodologies.

60.2 Limitations on Offer Amount

BMS is concerned that policies contained within Section 60, Negotiation Process, including but not limited to the process by which CMS will determine an offer, will de-value pharmaceutical advancements that are currently on the market and also result in even further chilling effects on future innovation. Given the novelty of this price setting program, CMS will face exceptional challenges in establishing the initial infrastructure to collect data and set prices.

To preserve patient access to innovation, BMS generally believes that the MFP should always be at or near the MFP ceiling—that is, the higher of the sum of the plan specific enrollment weighted amounts or the applicable percent of the non-FAMP—for each selected product. BMS also urges CMS to carefully consider situations where issues of patient access or preservation of incentives for innovation demand that a selected drug should be paid at the MFP ceiling. To help preserve patient access and engage in a fair and transparent process, BMS recommends that, at a minimum, CMS set all MFPs at the MFP ceiling price for IPAY 2026. Should CMS choose *not* to set prices at the MFP ceiling price, we offer several situations for CMS to consider below which we believe warrant special consideration.

- **MFP at Ceiling Price when Patient Access Imperiled:** In negotiating the MFP, there may be particular instances where a manufacturer demonstrates that setting the MFP below a particular price would imperil patient access to the selected drug. Research has shown that government-imposed pricing restrictions can discourage innovation and impede patient access to needed therapies.⁴¹ We urge CMS to ensure that patient access is a paramount consideration in negotiations with manufacturers when setting the MFP. In doing so, CMS should give significant weight to any evidence offered by a manufacturer that the setting of an MFP below a particular price would hinder patient access, and specify that, in such cases, the MFP will not be set below the lower of such price or the MFP ceiling price.
- **MFP at Ceiling Price for Initial Years into which Patent Protection Exists:** CMS should not set the MFP for selected drugs below the MFP ceiling price into which patent protection extends. BMS disagrees with CMS' position that it might adjust the price downward if the selected drug has patents or exclusivities that will last for a number of years. We ask CMS to place significant weight on whether, based on information submitted by the manufacturer, the selected drug will have any remaining patent protection at the start of the price applicability period. Given that a patent protection period can extend beyond a regulatory exclusivity period, we note that it may very well be the case that there will be remaining patent protection for a selected drug that extends into the price applicability period. To support continued innovation, we ask CMS to honor any remaining patent period for selected drugs by specifying that the MFP will not be set below the MFP ceiling price for any year of the price applicability period into which the drug's patent protection period extends. In this regard, we note that the Guidance suggests that an extended patent protection could serve as a reason to revise the "preliminary price" downward. That, too, would intrude upon patent protection in a way that Congress did not envision.

⁴¹ D. Schulthess and H. Bowen, "The Historical Impact of Price Controls on the Biopharma Industry," *Vital Transformations* (Nov. 22, 2021); see, e.g., D. Acemoglu & J. Linn, Market Size in Innovation: Theory and Evidence from the Pharmaceutical Industry, *Q. J. OF ECON.*, Vol. 119 (2004); see T. Abbott & J. Vernon, The Cost of US Pharmaceutical Price Reductions: A Financial Simulation Model of R&D Decisions, 28 *MANAGERIAL & DECISION ECON.* 293 (2007).

- **MFP at Ceiling for a Small Molecule Parity:** To help preserve small molecule innovation in parity with large molecule innovation, CMS should set the MFP for a drug (small molecule) at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval. We are concerned that the nine- and 13-year distinction arbitrarily promotes large molecule biologic innovation to the detriment of small molecule drug innovation. Disincentivizing manufacturers from investing in small molecule drugs presents serious risk to patient access to effective treatment. CMS should promote small molecule drug development to the greatest extent possible by counterbalancing the incentives that place a disproportionate emphasis on biologics development at the expense of small molecule drug development.
- **MFP at Ceiling for Preference on Medical Guidelines:** If a medication is listed as a preferred choice in medical guidelines for any indication, CMS should default to the ceiling price in recognition of the innovation, based on scientific rigor, that that product brings to patients and the health care system. Clinical practice guidelines are developed through a systematic review of evidence and careful consideration of a treatment's benefits/disadvantages compared to alternative therapies. Guidelines are developed by "a knowledgeable, multidisciplinary panel of experts and representatives from key affected groups" and take care to consider a thorough and wide range of perspectives as recommendations are developed.⁴² Additionally, guidelines committees reconsider and re-evaluate recommendations whenever new evidence is brought forward, assuring the medical community that patient care is held to the highest, safest, most evidence-based standards.
- **MFP at Ceiling for States Referencing MFP:** Multiple states have proposed or enacted legislation that would (or could) result in the state using a selected drug's MFP as a reference point in setting a pricing or payment limit that would apply to commercial or other non-Medicare markets.⁴³ Extending the MFP beyond Medicare markets would fundamentally disrupt the careful balance under the price setting program. Congress did not intend for this program to grind the wheels of medical innovation to a halt, and the scope of the MFP is limited accordingly. CMS should recognize the importance of protecting incentives for innovation by mitigating the harmful impact of the expansion of the MFP beyond the Medicare market and, thus, outside of that contemplated under the statute. To mitigate these serious concerns (and consistent with the statutory requirement to consider research and development costs as part of price setting), CMS should specify that the MFP will not be set below the MFP ceiling price where the manufacturer shows that the MFP will be used as a reference point in setting a pricing or payment limit outside of the Medicare market under state law, regulation, or policy.

60.2.2 Sum of Plan Specific Enrollment Weighted Amounts

In calculating the sum of plan specific enrollment amounts for selected drugs, CMS intends to use Part D PDE and Direct and Indirect Remuneration (DIR) data reported by plan sponsors.

As a preliminary matter, BMS asks CMS to clarify that the "plan specific enrollment weighted amount" does not include price concessions from manufacturers unless passed through at the point-of-sale. This clarification is necessary to align section 1194(c) with CMS' long-standing policy regarding the Part D negotiated price. Congress specifically defined "plan

⁴² Ernesto Guerra-Farfan et. al. "Clinical practice guidelines: The good, the bad, and the ugly" (Jan. 29, 2022), available at [https://www.sciencedirect.com/science/article/abs/pii/S0020138322000778#:~:text=Clinical%20practices%20guidelines%20\(CPGs\)%20play,in%20a%20time%20efficient%20manner](https://www.sciencedirect.com/science/article/abs/pii/S0020138322000778#:~:text=Clinical%20practices%20guidelines%20(CPGs)%20play,in%20a%20time%20efficient%20manner).

⁴³ See, e.g., S.B. 967, Va. Gen. Assembly (2023) (providing that the prescription drug affordability board "may adopt the Medicare maximum fair price ... for a prescription drug product as the upper payment limit amount"); H.F. 17, Minn. Leg., 93rd Sess. (2023) ("When setting an upper payment limit for a drug subject to the Medicare maximum fair price under United States Code, title 42, section 1191(c), the board shall set the upper payment limit at the Medicare maximum fair price.").

specific enrollment weighted amount” by reference to the “negotiated price” of the drug under Part D.⁴⁴ In turn, CMS regulations define the Part D “negotiated price[]” to be “inclusive of all price concessions from *network pharmacies*, except those contingent price concessions that cannot reasonably be determined at the point-of-sale,” but, notably, does **not** include price concessions from manufacturers.⁴⁵ Accordingly, there is no requirement that this price reflect price concessions from non-pharmacy third-parties, such as manufacturers.⁴⁶ Rather, PDPs and MA-PDs “may” choose whether to include manufacturer price concessions in the Part D negotiated price, to the extent they are made available at the point-of-sale. As CMS puts it: “Part D sponsors are allowed, but generally not required, to apply rebates and other price concessions at the point of sale to lower the price upon which beneficiary cost-sharing is calculated.”⁴⁷

Further, BMS notes that it does not have access to these data sources, and we request that CMS provide access to enable manufacturers to independently verify and reproduce calculations of plan specific enrollment weighted amounts for selected drugs.

While BMS appreciates CMS’ analysis of monthly Part D plan enrollment changes during 2022 to identify months with the lowest enrollment fluctuations (*e.g.*, December) for purposes of computing the sum of plan specific enrollment weighted amounts, we encourage the Agency to consider enrollment data encompassing the totality of calendar year to account for any significant fluctuations in the overall enrollment (*e.g.*, Medicare enrollees may change their prescription drug coverage at multiple points throughout the year, such as through Open Enrollment, as newly-eligible beneficiaries, or if utilizing the low income subsidy). As CMS is evaluating the PDE records for the full calendar year, we believe that the enrollment input should match that same period. Therefore, given the multiple opportunities for member enrollment changes throughout the year, it would be more appropriate for the Agency to use the full calendar year as an input in the sum of plan specific enrollment weighted amounts to avoid unnecessarily skewing the results.

60.2.3 Average Non-Federal Average Manufacturer Price

BMS notes that the statute defines extended-monopoly and long-monopoly drugs by reference to whether 12 or 16 years have elapsed since the initial FDA approval, but the statute is silent as to whether manufacturers should count 12 or 16 years to (1) the selected drug publication date; or (2) the start of the IPAY (which is generally 2 years after the selected drug publication date). In its Guidance, CMS appears to also be inconsistent on this point and seems to apply the length of time one way when describing the Initial Delay Request made by a biosimilar manufacturer (*i.e.*, to the start of the IPAY)⁴⁸ and another when determining the monopoly type as well as applicable percent specified for the purposes of establishing a ceiling price (*i.e.*, to selected drug publication date).⁴⁹ BMS requests that CMS provide clarity and consistent application that allows for transparency and planning.

⁴⁴ SSA § 1194(c)(2).

⁴⁵ 42 C.F.R. § 423.100 (emphasis added). CMS has recently promulgated a rule that will revise the definition of “Part D negotiated price” effective January 1, 2024. However, the revisions do not alter the fact that manufacturer price concessions are excluded from the Part D negotiated price. The new definition will require that the Part D negotiated price made available at the point of sale “include[] all price concessions ... from network pharmacies or other network providers,” including performance-based price concessions from pharmacies that may not be confirmed at the point of sale. 87 Fed. Reg. 27,704, 27,899 (May 9, 2022) (emphasis added).

⁴⁶ See also 87 Fed. Reg. at 27,835 (the Part D negotiated price is “the price paid to the network pharmacy or other network dispensing provider for a covered Part D drug dispensed to a plan enrollee that is reported to CMS at the point of sale by the Part D sponsor”).

⁴⁷ *Id.* at 27,835.

⁴⁸ See Guidance at 17 (“As such, Biosimilar Manufacturers may submit an Initial Delay Request for initial price applicability year 2026, provided that the Reference Drug named in the request will have been licensed for between 12 and 16 years prior to the start of the initial price applicability year on January 1, 2026.”).

⁴⁹ See *id.* at 45 (“The first approval date under section 505(c) of the FD&C Act or the first licensure date under section 351(a) of the PHS Act, as applicable, associated with the initial FDA application number for the active moiety / active ingredient (or fixed combination drug) must be on or before September 1, 2007.”).

Specifically, on CMS' proposed process in 60.2.3, we seek the following clarifications and recommendations:

- In steps 1 through 11, we ask CMS to clarify when "unit" refers to the non-FAMP unit (e.g., tablets) versus the PDE unit (e.g., milligrams). We also ask CMS to clarify when "non-FAMP" price refers to the entire NDC-11 package, one non-FAMP unit, or one PDE unit. We find that step 9 is particularly unclear on this.
- BMS appreciates CMS' clarification that no selected drug would be considered an extended-monopoly drug for purposes of negotiation prior to initial applicability year 2030. BMS understands that such drugs or biologics will be treated as short-monopoly drugs for the purposes of applying the applicable percent specified in section 1194(c)(1)(C) of the Act (that is 75% of non-FAMP).⁵⁰
- In addition to adjusting non-FAMP for CPI growth for the 12 months ending September 2022,⁵¹ CMS should also adjust for CPI growth for the 12 months ending September 2023. September 2023 CPI will be released on October 12, 2023. While this will be after the October 2, 2023, deadline for manufacturer data submission, it will be available for CMS' use in generating the ceiling price.

60.3.1 Identifying Indications for the Selected Drug and Therapeutic Alternatives for Each Indication

BMS supports CMS' decision to consider FDA-approved resources when identifying indications for a selected drug as well as the body of information that will be considered (manufacturer/public data, clinical guidelines, peer reviewed studies) when identifying therapeutic alternatives. As CMS prepares to examine a large volume of evidence across multiple indications and multiple therapeutic alternatives within each indication and conduct several simultaneous assessments, **BMS strongly recommends that CMS plan for additional dialogue with manufacturers, who have the most expertise with the selected drug, or at minimum, issue advance notice about the possible selection and the therapeutic alternatives that are likely to be considered by the Agency.**⁵² BMS also requests the opportunity to submit comparative effectiveness evidence data *after* CMS has identified indications and therapeutic alternatives.

In ex-U.S. countries, value assessments are typically conducted for a single indication and pricing and access mechanisms are subsequently applied behind the scenes to account for the differential benefit of each indication. But these mechanisms often have data collection and financial flow issues.⁵³ CMS should expect similar operational challenges to translate varying indication values to a single MFP—for example, oncology therapies can have dozens of indications, and the value story across these indications is unique given unique patients' needs; and for fixed-dose combinations, as well as single agents used in combination, value assessments have additional complexity. The consequences of inaccurate value determination can lead to restricted patient access to combination therapies. To prepare for this unprecedented task within a short amount of time with essentially no framework or examples on which to rely, **BMS recommends that CMS plan for additional consultation with stakeholders.**

60.3.2 Developing a Starting Point for the Initial Offer

BMS strongly objects to the use of the FSS or Big 4 price as a reference point for the initial offer. CMS' use of non-FAMP in section 60.2.3 already leverages the basic calculations underlying FSS and Big 4 prices. By also referring to final FSS and Big 4 prices, CMS would be capturing complexities of those calculations that should not apply. For instance, FSS and Big 4 prices can be heavily influenced by short-term commercial discounts and thus would serve as an inappropriate benchmark for setting a longer-term price. Further, reference to FSS and Big 4 prices in the final Guidance could have

⁵⁰ *Id.* at 44.

⁵¹ *Id.*

⁵² For example, in Germany, the Gemeinsamer Bundesausschuss (G-BA) offers pharmaceutical companies the opportunity of consultation prior to the beginning of benefit assessment procedures, relating to the appropriate comparator and the documents and studies to submitted.

⁵³ Office of Health Economics, "The Debate on Indication-Based Pricing in the U.S. and Five Major European Countries" (May 2018), available at <https://www.ohe.org/wp-content/uploads/2018/05/OHE-IBP-Final-Report-May-2018-Revised.pdf>.

the unintended consequence of reducing or eliminating manufacturer voluntary discounts that lead to lower prices for those government channels.⁵⁴

BMS is also concerned that the language for describing when CMS would leverage FSS and Big 4 prices is very unclear. As currently written, one of the three situations which would lead to use of these prices as the starting point for the initial offer is “if there is a single therapeutic alternative with a price above the statutory ceiling.”⁵⁵ It seems that this would always be likely to occur and would further signify that the statutory ceiling has *already* been reduced to a more competitive price than the therapeutic alternative. This would make referencing FSS or Big 4 price unjustified.

CMS proposes to begin developing a starting point for the initial offer by identifying therapeutic alternatives within the same drug class based on properties such as chemical class, therapeutic class, or mechanism of action before considering other classes. This broad Guidance could potentially allow inclusion of outdated technologies and generic drugs as therapeutic alternatives. BMS strongly objects to the inclusion of generics and biosimilars in the basket of therapeutic alternatives and notes that if CMS determines a generic to be the appropriate therapeutic alternative to a drug, then *de facto* that drug should not be considered single sourced for the purposes of drug selection criteria.

60.3.3 Adjusting the Starting Point Based on Clinical Benefit

BMS appreciates CMS’ decision to broadly evaluate the body of clinical evidence submitted by manufacturers and the public to determine the clinical benefit of a selected drug and therapeutic alternatives. We commend CMS’ intent to use a qualitative approach to preserve flexibility to consider nuanced differences. To ensure the proper consideration of information between a selected drug and alternatives, **manufacturers should have insight into CMS’ literature review and the opportunity to comment on the accuracy of the proposed value capture.**

When considering evidence about alternative treatments and added benefits of a selected medicine, BMS also encourages CMS to consider several critical elements in order to capture the full- and long-term value of a treatment, including: clinical outcomes, medical association guidelines, and health equity and subpopulation benefits. **Equally important as the clinical benefits are the non-clinical health outcomes and benefits**, including but not limited to, reduction in burden to the health care system, patient preferences, treatment adherence, and scientific spillover. **Non-clinical benefits should be weighted heavily when determining the starting point for the MFP offer.** Also, important to consider is situations in which medicines treat conditions with a limited number of treatment alternatives, as well as the innovation and societal progress that is achieved in treating serious medical conditions, including incremental success achieved to address unmet needs and provide hope for patients.

60.3.3.1 Analysis for Selected Drugs with Therapeutic Alternative(s)

BMS supports CMS’ intent to analyze a full body of qualitative information when reviewing the clinical benefit and encourages CMS to go beyond outcomes and safety profiles of the selected drug and therapeutic alternatives to deeply consider a robust body of information when assessing a selected drug’s impact on unmet need and therapeutic advance.

CMS intends to define unmet need as treating a disease or condition in cases where very limited or no other treatment options exist. This is an unduly restrictive definition of unmet need. As CMS will assess medications in the middle of their lifecycles, BMS recommends that unmet need be considered from initial approval to the time of assessment. Additional value should be particularly considered for those medications that treat serious medical conditions, including those that

⁵⁴ CMS may remember a similar situation that occurred after the creation of Best Price in the MDRP that resulted in market distortions, unintended consequences, and the need for additional federal legislation. See Nicholas C. Fisher, The 340B Program: A Federal Program in Desperate Need of Revision After Two-And-A-Half Decades of Uncertainty, 22 J. Health Care L. & Pol’y 25 (2019).

⁵⁵ Guidance at 49.

make incremental steps toward curative goals. Further, unmet need should be viewed from the perspective of patients and providers. Unmet need should accordingly encompass a spectrum of characteristics, such as: alternative dosing regimens; route of administration; reduction of side effects; and shorter treatment periods.

60.3.3.2 Analysis for Selected Drugs Without Therapeutic Alternatives

As conveyed elsewhere, BMS strongly disagrees with CMS' proposal in 60.3.2 to determine the starting point of a selected drug with no therapeutic alternative based on the FSS or Big Four price if they are below the statutory ceiling. BMS believes unmet need warrants a starting price of the ceiling price in these situations.

60.4.1 Provision of an Initial Offer and Justification

It is critical for manufacturers to understand the context and basis for the MFP offer. To increase transparency and further CMS' two-way dialogue with a manufacturer of a selected drug, we urge the Agency to consider releasing a confidential report for the manufacturer alone alongside the initial offer and justification to better inform manufacturer counteroffers and subsequent data submissions. Given the anticipated submissions from members of the public, including academic experts and clinicians, CMS will have a significant amount of information on a selected drug, as well as latitude in determining what is included in an initial concise justification. Manufacturers are unlikely to have enough context to effectively address potential evidence gaps in the initial offer, which would impact manufacturers' abilities to craft an appropriate, evidence-based counteroffer. **We therefore ask the Agency to provide a confidential report to manufacturers with details on the Agency's assessment of a selected product, as well as the evidence which was deemed relevant and appropriate from stakeholder submissions.** The concise justification and report should, at a minimum, include the following information: (1) evidence sources CMS considered, including third-party assessments the Agency may have formally or informally considered; (2) how each factor was weighted in CMS' MFP determination; (3) how patients and other stakeholders engaged in the process and influenced CMS' decision-making; and (4) benefits and impacts that CMS considered.

60.4.3 Negotiation Process After Manufacturer Counteroffer

BMS has serious concerns with CMS' process for interfacing with manufacturers of selected drugs. As set forth in the Guidance, manufacturers may have up to three meetings with CMS—all occurring *after* the initial MFP is set by the Agency. While we agree with CMS that meetings occurring after CMS rejects a manufacturer's counteroffer is necessary and will allow for a more efficient and effective process, starting meetings only after rejection of the manufacturer counteroffer is too late. In our vast experience negotiating with states and payers, the proposed process is highly unusual and arbitrary.

BMS strongly believes that CMS should meet with the manufacturer of a selected medicine at *multiple points* during the "negotiation" process to allow manufacturers to address questions and provide additional commentary on the value of these medicines. **At a minimum, we urge CMS to meet with manufacturers during six discrete periods in the value assessment process—but without limitation on the number of meetings deemed necessary by the parties:** (1) prior to drug selection; (2) after drug selection but prior to initiation of the "negotiation" process; (3) immediately after manufacturer data and evidence submissions; (4) prior to CMS presenting initial MFP offer; (5) after CMS presents the initial offer; and (6) after a counteroffer is made.

60.5 Application of the MFP Across Dosage Forms and Strengths

Regarding how CMS intends to apply the MFP across dosage forms and strengths, BMS finds Steps 1 through 10, describing the process to apply final MFPs to NDC-11s, to be very unclear. Similar to comments on 60.2.3, we believe the term "unit" sometimes refers to non-FAMP unit (e.g., tablets) and sometimes refers to PDE unit (e.g.,

milligrams).⁵⁶ Where Steps 1 through 4 refer to NDC-9, we believe the intent is NDC-11.⁵⁷ The term “dosage form and strength” appears to refer to the NDC-9 level in step 1, but the NDC-11 level in step 10.⁵⁸ Additional clarity will be needed to understand this section.

60.5.1 Application of the MFP to New NDAs/BLAs or NDCs

We seek to reiterate our strong opposition to CMS’ policy at 30.1 to identify “qualifying single source drugs” at the active moiety/active ingredient level. BMS believes that this policy is contrary to and beyond the scope of the IRA statute, creates unnecessary confusion in the face of statutory clarity, departs from well-established means of identifying distinct products, and will be detrimental to future innovation.

Section 80 – MFP Eligible Individuals

BMS seeks clarification on the definition of “MFP Eligible Individuals” in Section 80, particularly as it relates to Part D enrollees. For drugs furnished under Part B, an MFP-eligible individual is one who is enrolled under Part B (and applicable Part C plans) and if *payment* may be made under Part B for such selected drug.⁵⁹ For drugs furnished under Part D, an MFP-eligible individual is one who is enrolled under Part D (and applicable Part C plans) and if *coverage* is provided by a Part D plan for such selected drug.⁶⁰ We also interpret coverage to mean that a selected drug was billed.

We note that the subtle difference in CMS’ language—payment versus coverage—matters. Take, for example, a situation in which a Part D patient opts *not* to use insurance for a selected drug. The drug is covered and provided to the patient, and based on CMS’ proposed definition, we take this to mean that a manufacturer would still have to provide the MFP on that drug because the patient would be an eligible individual. Manufacturers need certainty, such as through claims data, to verify that MFP eligible individuals are receiving MFP drugs at the MFP. This gap in CMS’ definition makes it more difficult for stakeholders to ensure accuracy and operational success.

BMS asks CMS to modify and/or clarify the definition of a Part D-eligible individual to be consistent with the approach for Part B, specifically, an individual who is enrolled under Part D and if *payment* is provided under Part D for such selected drug. In effect, this could mean that in order for a manufacturer to offer the MFP for a selected drug, that drug must be billed as a Part D (or applicable Part C) product. We look forward to CMS clarifying this topic in its updated Guidance.

Section 90 – Manufacturer Compliance and Oversight

90.2 Monitoring of Access to the MFP

BMS encourages CMS to support manufacturers in providing access to the MFP by mandating that providers seeking to benefit from the MFP must report a minimally necessary data set to the manufacturer or its vendor for the purposes of MFP discount validation in a timely manner, according to standard business practices, and in alignment with non-duplication requirements. CMS should expressly acknowledge that manufacturers may establish, receive, review, and as necessary, audit MFP validation data to ensure manufacturers have provided MFP access in accordance with the statute. CMS should also mandate that providers submit MFP validation data. As mentioned in our comments to section 40.4

⁵⁶ *Id.* at 44.

⁵⁷ *Id.*

⁵⁸ *Id.*

⁵⁹ *Id.* at 63 (emphasis added).

⁶⁰ *Id.*

and 40.4.1, it would be otherwise impossible for the manufacturer, much less CMS, to ensure access to the MFP consistent with statutory requirements.

Relatedly, CMS also acknowledges that “CMS intends to leverage existing mechanisms to ensure that ... the MFP for a selected drug is provided only to MFP-eligible individuals.”⁶¹ CMS notes that each Medicare Part D plan has a unique processor identification number (RxBIN)/processor control number (PCN), which will ensure that the pharmacy is able to identify at the point-of-sale whether the individual is an MFP-eligible individual.⁶² BMS requests similar access to this type of standard information in its requests for data to validate the discount extension. CMS need not prescribe the data set; rather, the Agency should provide the manufacturer with the flexibility to determine the data necessary to validate the MFP discount. Regarding the example included in the Guidance, the manufacturer would be unable to validate that the individual was an MFP-eligible individual, as no data is provided to the manufacturer through the chargeback system to validate such an MFP transaction.

CMS also acknowledges that “the private sector may make modifications to these existing mechanisms [chargeback or rebate] to effectuate access to the MFP.”⁶³ Such changes are not only possible, but they would be absolutely necessary, as the current chargeback system does not contain the proper data elements to accurately and appropriately extend the discount. BMS therefore urges CMS to make clear that providers must submit the reasonable data requested by a manufacturer, consistent with the data manufacturers would request under standard business practices.

CMS also solicits feedback on a process by which stakeholders could report to CMS instances of failure to provide MFP access.⁶⁴ CMS should consider the paramount role of data to support its efforts. Absent transactional data, CMS will be challenged to accurately “investigate reports of potential noncompliance, and if appropriate, impose CMPs on the... manufacturer.”⁶⁵ It is unclear what CMS believes the Agency will use to investigate and impose fines, absent an expectation for providers to submit data, and absent CMS’ access to that data. Additional rationale for CMS’ role in clarifying its expectation for providers to submit MFP validation data is provided in response to sections 40.4 and 40.4.1

BMS requests clarification regarding what CMS intends by stating: “Should it subsequently be determined that the 340B ceiling price is lower than the MFP for the selected drug, the manufacturer would have to provide to the covered entity the difference between the MFP and the 340B ceiling price.”⁶⁶ Because the ceiling price is calculated quarterly, the only time a ceiling price is “subsequently determined” to be a different price than its quarterly price is pursuant to a pricing restatement. We presume that is the context for CMS’ statement, but seek confirmation on this point. CMS should confirm that it is not using the “subsequently determined” language to attempt forcing an extra-statutory obligation on a manufacturer to offer 340B discounts pursuant to a 340B replenishment model for an infinite period of time in the future.

90.4 Monitoring for Bona Fide Marketing of Generic or Biosimilar Product

BMS opposes this proposal of continued monitoring for whether “robust and meaningful competition exists in the market” for a given drug. This approach is found nowhere in the statute and would violate the statute’s clear command as to exclusion from drug selection.

⁶¹ *Id.* at 65.

⁶² *Id.*

⁶³ *Id.*

⁶⁴ *Id.* at 66.

⁶⁵ *Id.*

⁶⁶ *Id.*

The IRA “negotiation” framework applies only to a single source product, meaning that if a different source exists (i.e., a generic or biosimilar), the product categorically cannot come from a single source. Further, the plain meaning of the statutorily unqualified term “marketed” reveals that Congress did not contemplate extra-statutory concepts related to degree of utilization or “robust and meaningful” competition.

Both CMS and FDA, in established contexts Congress would have understood, have long determined a product to have been marketed based on a point-in-time standard. For instance, CMS has long used this concept in the MDRP, where “market date” has been defined in guidance to mean “the earliest date the drug was first marketed under the application number of any labeler,”⁶⁷ and where “marketed” is defined under the National Drug Rebate Agreement to mean the date on which the product was first “available for sale by a manufacturer in the states.”⁶⁸

Interposing subjective, indefinite criteria in the determination of when a generic is “marketed” is inappropriate, subject to abuse, ultra vires, and inconsistent with the terms of the statute. BMS therefore supports CMS taking a position that aligns with the “market date” reported under the MDRP because it presents an established, uniform standard that would help ensure that manufacturers are not inappropriately subject to selection, negotiation, application of an MFP, or an excise tax. Adopting this standard would also help ensure clarity and consistency in the identification of these key dates under Medicare price setting.

BMS urges CMS to use this standard for identifying both: (1) the date on which a generic or biosimilar is first marketed; and (2) the date on which CMS determines that to be the case.

Section 100 – Civil Monetary Penalties

While dictated by statute, the CMPs associated with the IRA “negotiation” framework are virtually unparalleled in magnitude and strongly warrant CMS implementing special safeguards against erroneous and inappropriate application. BMS asks that CMS provide manufacturers with notice of any preliminarily identified deficiency and at least 30 days to cure such deficiency before any sanction is imposed. In addition, CMS should provide manufacturers with a reasonable opportunity to dispute CMS’ findings prior to the imposition of any sanction to better ensure that sanctions are not imposed based on legal or factual errors by the Agency.

First, the raw magnitude of the penalties under the statute warrant implementation of such pre-sanction procedural safeguards. It is vital that CMS rely on penalties as an enforcement mechanism only when doing so is clearly warranted, and not for minor mistakes or inadvertent errors. As such, penalties should be imposed only if they are found to be appropriate following the completion of a reasonable dispute resolution process, and if deficiencies persist after a manufacturer has been given a reasonable opportunity (at least 30 days post-notice) to cure the alleged deficiencies.

Further, pre-sanction procedural safeguards play a critical role in reducing the risk of erroneous deprivations of property. CMPs could be in the hundreds of millions of dollars, raising fundamental concerns of due process of law if CMS were to impose penalties of this enormity without any mechanism for meaningful pre-deprivation review.⁶⁹

Pre-sanction procedural safeguards are also warranted in light of the complexity and newness of the price setting program. It is inevitable that there will be significant ambiguity with respect to program requirements, especially in the

⁶⁷ CMS, MDRP Data Guide § 5.15 (Apr. 2022).

⁶⁸ National Drug Rebate Agreement § I(I), 83 Fed. Reg. 12,770 (Mar. 23, 2018).

⁶⁹ See generally *Matthews v. Eldridge*, 424 U.S. 319 (1976) (factors for evaluating when due process requires a pre-deprivation hearing include the nature and magnitude of the private interest affected and the risk of an erroneous deprivation, along with any implicated governmental interest).

early years of implementation. As such, manufacturers will necessarily be seeking to comply with requirements in a landscape of marked uncertainty. In these circumstances, it would be patently unreasonable if, for example, CMS began imposing vast monetary penalties (e.g., \$1 million per day) due to inadvertent technical mistakes or innocent misunderstandings.

Additionally, it bears noting that there is ample precedent for CMS establishing similar safeguards in analogous contexts. For example, just recently, CMS established a multi-layered dispute resolution process under the new Medicare Part B discarded drug refund process. That process is specifically intended to allow for resolution of issues *before* the issuance of any final invoice. In implementing this process, CMS acknowledged that, while not expressly required by statute, “proactively establishing such a process [would] aid in the successful implementation of [the law].”⁷⁰

CMS has the legal authority to implement the requested safeguards. CMS has broad discretion with respect to implementing mechanisms to “monitor compliance by a manufacturer with the terms of a [Drug Price Negotiation Program] agreement.”⁷¹ The pre-sanction dispute resolution and notice-and-cure processes are both types of compliance monitoring mechanisms that CMS has clear statutory authority to implement.

Section 110 – Part D Formulary Inclusion of Selected Drugs

BMS agrees with CMS that the statute requires a selected drug, for which an MFP is in effect, to be on all Part D formularies. We note that it is critical for CMS to recommend, and health plans to design, formularies that promote beneficiary access to *all* medicines, both MFP and non-MFP medicines.

BMS is concerned with how onerous formulary management policies may impede access to care, particularly in light of government price setting, and we are disappointed that CMS did not address how price setting might have unintended downstream consequences for the Part D program, including plan competition dynamics and increased utilization management (UM), and, most of all, for patients. We urge CMS to critically examine these impacts and prioritize shared decision-making between patients and providers, not health plans, on appropriate treatment plans.

In general, BMS supports public policies that ensure that health plan UM techniques follow clinical guidelines, provide timely and transparent responses to patients, and allow for physician/patient choice based on individual patient medical needs and desired outcomes. While UM techniques, such as step therapy and prior authorization policies, are purportedly designed to manage drug costs, these UM practices can lead to medication adherence issues, delayed access to medications, negative health outcomes for patients, and increased administrative burden. Delays in effective treatment can increase costs to the health care system and cause patients to suffer unnecessarily.⁷² Excessive UM hurdles can also result in delays in access, increase administrative burden, diminish clinical autonomy, lower job satisfaction, and exacerbate feelings of burn-out for health care providers.⁷³

UM techniques also disproportionately impact communities of color, further exacerbating existing health disparities. In a survey of over 3,600 patients, majorities of Hispanic Americans (64%) and Black Americans (55%) report being subject to

⁷⁰ 87 Fed. Reg. 69,404, 69,731 (Nov. 18, 2022).

⁷¹ SSA § 1196(b).

⁷² See Strand V, Tundia N, Song Y, Macaulay D, Fuldeore M. Economic Burden of Patients with Inadequate Response to Targeted Immunomodulators for Rheumatoid Arthritis. *J Manag Care Spec Pharm*. 2018 Apr;24(4):344-352 and Avalere Health, Step Therapy Can Lead to Higher OOP Costs for Crohn’s Disease Patients (October 2020), available at <https://avalere.com/insights/step-therapy-can-lead-to-higher-oop-costs-for-crohns-disease-patients>.

⁷³ AMA, 2021 AMA prior authorization (PA) physician survey, available at <https://www.ama-assn.org/system/files/prior-authorization-survey.pdf>.

at least one UM barrier to accessing medicines, compared to 44% of White Americans.⁷⁴ Many physicians of color also recognize the impact of UM on their minority patients; in a survey by the Association of Black Cardiologists, physicians agree “very much” that prior authorization contributes to delays in care (61%), higher patient confusion (50%), increased medication discontinuation (45%), reduction in medication adherence (32%), and worse outcomes (16%).⁷⁵

While not contemplated in the Guidance, we also urge CMS to think critically about how Part D redesign will affect patient access to MFP and non-MFP medicines. In fact, BMS asserts that reforms to UM are even more critical in light of Part D redesign; for these new Part D redesign changes to produce the desired outcome for enhanced patient access, the Part D program must maintain its competitive, market-based structure. As health plans assume significantly greater liabilities as a result of the IRA, BMS is concerned they may employ more aggressive UM techniques to restrict patient access to medically necessary care. Historically, plans have used creative formulary design, onerous prior authorization schemes, and step therapy delays to limit plan liabilities, all of which adversely affect enrollees’ access to medicines. BMS is concerned that without appropriate guardrails and patient protections against UM, many of these trends may be exacerbated under the new Part D benefit design, which would run counter to the intent of the redesign policy.

BMS urges CMS to critically consider the potential downstream impacts of government price setting on Part D plan dynamics and patient access. We assert that it is necessary for the Agency to contemplate these issues further in future guidance and rulemaking processes.

Section 120 – Application of Medicare Part B and Part D Prescription Drug Inflation Rebate Programs to Selected Drugs

CMS Should Clarify That a Selected Drug is Not Subject to an Inflation Rebate: CMS asserts: “The Part B and Part D inflation rebate programs apply to selected drugs, regardless of the status of the drug as a selected drug. Alternatively said, whether a drug is a selected drug will have no bearing as to whether the drug is also subject to the Part B and Part D inflation rebate programs.”⁷⁶ This assertion, however, is incorrect, and we ask CMS to clarify a selected drug is not subject to an inflation rebate.

By statute, the Part B inflation rebate calculation is based in relevant part on the amount by which “106 percent of the amount determined under paragraph (4) of [section 1847A(b) of the SSA for [a part B rebatable drug] during the calendar quarter... exceeds [] the inflation-adjusted payment amount... for such part B rebatable drug during the calendar quarter.”⁷⁷ Notably, the circumstances under which an amount is “determined” under paragraph (4) is dictated by section 1847A(b)(1) (*i.e.*, paragraph (1)).⁷⁸ Specifically, paragraph 1 dictates a payment amount of, “in the case of a single source drug or biological... , 106 percent of the amount determined under paragraph (4) or in the case of such a drug or biological product that is a selected drug... , 106 percent of the amount determined under paragraph (4) or in the case of such a drug or biological product that is a selected drug... , 106 percent of the maximum fair price... applicable for such drug and a year during such period.”⁷⁹ In other words: a *selected* drug’s payment amount is determined under paragraph (1), which amount is determined without regard to paragraph (4). It is only the payment amount for a *non-selected* drug that is determined under paragraph (4). It necessarily follows that the Part B inflation rebate calculation has no application to a selected drug, as, with respect to such a drug, there is no

⁷⁴ PhRMA, “Covered By Insurance But Still Exposed: Barriers to Care for Insured Americans,” available at https://phrma.org/-/media/Project/PhRMA/PhRMAOrg/PhRMA-Org/PDF/P-R/PES-Report-2_final.pdf.

⁷⁵ Association of Black Cardiologists, “Identifying How Prior Authorization Impacts Treatment of Underserved and Minority Patients” (2019), available at <http://abcario.org/wp-content/uploads/2019/03/AB-20190227-PA-White-Paper-Survey-Results-final.pdf>.

⁷⁶ Guidance at 71.

⁷⁷ SSA § 1847A(i)(3).

⁷⁸ See *id.* § 1847A(b)(1).

⁷⁹ *Id.* § 1847A(b)(1)(B).

amount “determined under paragraph (4).” By the plain terms of the statute, a selected drug cannot be subjected to a Part B inflation rebate.

This is not surprising. A manufacturer should not be obligated to pay an inflation rebate on a selected drug because Medicare expenditures on a selected drug are constrained by the MFP. Thus, with respect to a selected drug, Medicare is shielded from the increase in expenditures occasioned by a price increase that outpaces inflation that an inflation rebate is intended to address. For these reasons, CMS should clarify that a selected drug is not subject to an inflation rebate.

Other Considerations

Diversion and “Spillover”

MFP Spillover Risks: BMS believes (and the statute requires) that the MFP that the government sets should be available to Medicare-eligible beneficiaries only, given that this policy is a Medicare policy intended to reduce prescription drug costs for Medicare patients. BMS, however, is highly concerned with how the scope of the MFP could potentially be expanded beyond the intended Medicare market (“spillover”).

The MFP risks spillover beyond Medicare in two ways: (1) diversion, where Medicare patient status is not established at purchase, risking MFP discount diversion to ineligible individuals; and (2) unintended reimbursement consequences, when commercial payers may seek to adjust to MFP-based reimbursement for non-MFP-eligible individuals, thus compromising patient access to therapies. Spillover risk is also present at the state level.

Diversion to Non-MFP Eligible Individuals: BMS supports the use of a method to effectuate the MFP that gives meaning to the MFP access provision by enabling manufacturers to confirm that a particular unit was in fact used for an MFP eligible individual and therefore in fact entitled to the MFP. To ensure transparency, it is even more important to have a robust mechanism for discount eligibility verification in place due to the lack of administrative and judicial review.

Unintended Reimbursement Consequences: BMS is concerned that due to financial and operational challenges related to utilizing MFP products, unintended reimbursement consequences will likely occur, resulting in treatment switches to non-MFP products, which could also jeopardize patient access to medicines.

We look forward to reengaging the Agency on this topic to ensure that providers remain financially whole, and patients receive the medicines that they need.

Rationale for Exclusion of MFP Units from Average Sales Price (ASP) Calculation: To protect patient access to critical medicines in non-Medicare markets, BMS urges CMS to exclude MFP units from the definition of “unit” for purposes of the ASP calculation. Although Medicare reimbursement for an MFP-eligible Part B medicine will not be based on ASP, non-Medicare payers commonly rely on ASP as a metric for setting reimbursement rates for such drugs. BMS is highly concerned that due to this dynamic, over time, the MFP will increasingly lower the ASP, and as a result, ASP-based reimbursement rates of non-Medicare payers will be increasingly insufficient to make providers whole for their acquisition cost of the selected drug. Moreover, there is real risk that patients insured by non-Medicare payers will not have access to these drugs. BMS asserts, therefore, that it is critical that CMS act to exclude MFP units from ASP to protect patient access to critical medicines in non-Medicare markets.

Fortunately, CMS has clear authority to avoid this serious concern by excluding MFP units from ASP. The ASP statute defines “unit” for ASP purposes to mean:

[W]ith respect to each National Drug Code (including package size) associated with a drug or biological, the lowest identifiable quantity (such as a capsule or tablet, milligram of molecules, or grams) of the drug or biological that is dispensed, exclusive of any diluent without reference to volume measures pertaining to liquids. **For years after 2004, the Secretary may establish the unit for a manufacturer to report and methods for counting units as the Secretary determines appropriate to implement this section.**⁸⁰

The statute expressly delegates broad authority to CMS to define “unit” for ASP purposes—and, notably, the legislative history of the statute reveals that Congress specifically intended the exclusion of “those sales that do not reflect market prices” from ASP.⁸¹ CMS has also previously exercised this authority to exclude specified units from ASP. For example, CMS has defined “unit” for ASP purposes to exclude Competitive Acquisition Program (CAP) units from ASP: CMS’ ASP regulations provide that “[t]he method of counting units excludes units of CAP drugs... sold to an approved CAP vendor... for use under the CAP....”⁸² By excluding CAP units from ASP, CMS excluded from ASP units with prices negotiated by vendors under a federal program that it rightly determined did not reflect market prices, thereby honoring Congressional intent. In doing so, CMS noted that ASP and CAP prices were “intended to be alternatives to each other” and, thus, CAP units should not be included in ASP.⁸³

BMS asserts that MFP units should not be included in ASP—namely, because the MFP is available only with respect to the Medicare market, under certain circumstances. MFP eligible individuals do not include non-Medicare beneficiaries, and, thus, BMS believes that the MFP does not reflect a market price that should be reflected in ASP. In addition, the MFP is an alternative to ASP—it is used in place of ASP to establish Medicare reimbursement rates for MFP-eligible Part B products. For this reason, too, CMS should exclude MFP units from ASP, as it did with CAP units.

To preserve provider reimbursement and ultimately patient access, BMS strongly urges CMS to exercise its authority to define “unit” for purposes of ASP to exclude MFP units from the ASP calculation.

Dispute Resolution Process

Despite stating that the Guidance would include a “dispute resolution process for specific issues that are not exempt from administrative and judicial review under section 1198,”⁸⁴ we are disappointed that CMS does not appear to contemplate such a process. BMS strongly believes that the statute does not prohibit CMS from establishing a dispute resolution process, and furthermore, there is strong policy and operational rationale for doing so.

Given the complexity of implementing a novel price setting program under exceedingly short timelines, as contemplated throughout our comments, there is a high likelihood that errors and disputes will occur, especially within the initial IPAYs. A process for rectifying disputes—including correction of errors in data and evidence interpretation—is therefore critical. To further transparency and accuracy, BMS urges CMS to not only create a dispute resolution process but do so in advance of the September 1, 2023, drug selection date.

⁸⁰ *Id.* § 1847A(b)(2)(B) (emphasis added).

⁸¹ See H.R. Rep. No. 108-391, at 587-88 (2003), reprinted in 1808 U.S.C.C.A.N. 1954-55.

⁸² See 70 Fed. Reg. 39,021, 39,077 (Jul. 6, 2005). See also 74 Fed. Reg. 61,738, 61,915 (Nov. 25, 2009).

⁸³ *Id.* at 61,915.

⁸⁴ CMS, “Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026” (Jan. 2023), available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf>.

Appendix C – Definitions for Purposes of Collecting Manufacturer Specific Data

Although the Guidance enumerates various manufacturer specific data that CMS “must” consider,⁸⁵ the Agency does not address with specificity how these factors will be considered to establish the MFP or adjust the preliminary price. BMS is highly concerned that the data elements that CMS has proposed to establish the MFP do not adequately capture the value of a drug on patients and the broader health care system. Furthermore, BMS continues to urge CMS to specify that the Agency will consider any information submitted by manufacturers as part of the price setting process, even if that information is not tied to a specific statutory factor.

Consistent across Appendix C, BMS recommends that CMS utilize a uniform starting point, and annually thereafter, across all data collections (*e.g.*, January 1, 2020), and *not* mandate information prior to this point absent manufacturer provision of such information. Said differently, BMS believes it is impractical for CMS to select arbitrary dates and timelines for reporting and urges the Agency to reconsider utilizing the nearest month or quarterly cutoff. We are concerned that without a firm date for a look-back period, it could disadvantage and unfairly penalize manufacturers for previous pricing practices and data collection before the law went into effect. Our comments on specific sections of Appendix C follow.

(a) Research and Development (R&D) Costs

Definitions for 1. R&D: Basic Pre-Clinical Research Costs

Based on CMS’ proposal, we believe that the Agency is not considering a full and complete appreciation for pharmaceutical development and has identified irrelevant and inappropriate factors for consideration. Compiling and calculating R&D costs for a drug that has been on the market for over a decade is a complicated process that is not easily reduced to a finite set of specific considerations, factors, or other items. BMS requests CMS to utilize an individual calendar year as a starting point for all manufacturers’ selected drug. We note that it is inappropriate to create a framework that not only considers historical or “lifetime”⁸⁶ data reflective of early research but also assumes that the manufacturer can access information that was not required to be captured and reported. Furthermore, requesting manufacturers to retrospectively collect asset-level pre-clinical data is not feasible. We urge CMS to consider a more precise method.

BMS seeks clarification on the data elements that would satisfy CMS’ inquiry on costs associated with “preparing the selected drug for clinical trials.”⁸⁷ Additional context is needed to determine if this requirement refers to manufacturing costs or costs associated with the drug development process, as CMS’ request is vague. Furthermore, in inquiring about costs tied to personnel, BMS believes it would be pertinent to present costs associated with both internal and external function service providers that are necessary in conducting the various studies associated with the selected drug. It is vital that CMS assess these costs in totality when determining the initial MFP price and consider all direct and indirect costs that the manufacturer incurs throughout the life cycle of the selected drug.

Definitions for 2. Post-Investigational New Drug (IND) Application Costs

Repeatedly, CMS refers to “personnel”⁸⁸ in Appendix C. BMS requests that CMS define “personnel” and explicitly consider both the internal and external function service providers that support and are directly associated with the study. Additionally, BMS encourages CMS to further clarify what the Agency means in reference to “preparing the

⁸⁵ Guidance at 52.

⁸⁶ *Id.* at 82.

⁸⁷ *Id.* at 84.

⁸⁸ *See id.* at 83, 84, 85, 87.

selected drug for clinical trials.”⁸⁹ We believe this phrasing is vague, and we are unclear if this includes the costs of the manufacturing and costs of developing the processes.

Definitions for 3. R&D: Completed U.S. Food and Drug Administration (FDA)-Required Phase IV Trials

BMS is concerned that CMS continues to demonstrate a lack of full understanding of pharmaceutical development and research. There are different types of clinical trials conducted post-FDA approval, and CMS needs to account for these factors.

Definitions for 4. R&D: Post-Marketing Trials

CMS needs to clarify the scope of post-marketing trials and specifically address if it includes investigator sponsored studies (ISR) and real-world data gathering. Typically, these are under the purview of medical generation evidence, also referred to as “post-marketing trials,” and BMS encourages CMS to further clarify its intent. Additionally, CMS must recognize and consider scenarios in which the manufacturer does not operate the study. BMS also asks CMS to provide guidance on how the Agency will consider alliances or co-development arrangements, and subsequently, how it intends for the manufacturer to consider this for reporting purposes.

BMS notes that CMS does not appear to fully recognize the additional costs directly associated with running clinical trials, and BMS urges CMS to explicitly identify and consider these costs, specifically the purchase of third-party assets, such as combination or comparator assets. BMS urges CMS to recognize and consider ongoing expenses post approval; for certain therapeutic areas, often oncology and hematology, there are costs related to continued follow-up and data generation. CMS must recognize the ongoing investment in and value of these products. Another factor that CMS should consider is the promotional costs to educate physicians on the benefit of the product, both U.S. and ex-U.S.

Definitions for 5. R&D: Abandoned and Failed Drug Costs

BMS strongly asserts that *all* clinical trials conducted by the manufacturer need to be considered by CMS, not only those that were approved. “Failed” clinical trials require significant capital from manufacturers and frequently can contribute to new discoveries—simply because a trial did not have a successful readout does not mean that the manufacturer did not incur expenses to develop the asset or make important scientific discoveries along the way. BMS urges CMS to consider the totality of the investment, including failed and approved clinical trials.

BMS urges CMS to recognize the tremendous financial burden that manufacturers will incur to report the overwhelming number of molecules and targets that do not proceed to Phase I or IND. Additionally, BMS requests clarification on how to report failed clinical trials.

Definitions for 6. R&D: All Other R&D Costs

BMS requests CMS to explicitly define “all other R&D costs.”

(b) Current Unit Costs of Production and Distribution of the Drug

Supplemental to BMS’ concerns in response to “Definitions for 1. R&D: Basic Pre-Clinical Research Costs,” CMS must consider removing data reporting elements for product and development costs at the asset level prior to a specific date. To reiterate, there may be instances where the manufacturer does not possess nor have access to such information due to previous reporting and tracking guidelines.

⁸⁹ *Id.* at 84.

Additionally, CMS requires the reporting of “allocated shared operating and other indirect costs (such as capitalized production facility costs, benefits, generalized and administrative costs, and overhead expenses) specific to each NDC-9 based on unit volume,”⁹⁰ but needs to also consider the other overhead expenses that are not allocated, like freight, global quality, and the supply chain organization.

BMS also requests that CMS consider expenses associated with non-manufacturing facilities that contribute to the cost of developing and marketing a selected drug.

(c) Patents, Exclusivities, and Approvals

BMS supports protection of intellectual property (IP) rights and believes that an effective IP framework is essential for the viability of the biopharmaceutical industry and efforts to deliver innovations that address unmet patient needs. The discovery and development of new medicines is a long, complex, and rigorous process. BMS is concerned that CMS’ proposals could contradict the framework that was intended to protect and encourage innovation, and strongly disagrees with CMS’ position that it may adjust the MFP downward if the selected drug has patents or exclusivities that “will last for a number of years.”⁹¹ As stated above, BMS believes that CMS should not set the MFP for selected drugs below the MFP ceiling price into which patent protection extends.

CMS requests that “all pending and approved patent applications, including expired and non-expired approved patents submitted, sponsored, licensed, and/or acquired the Primary Manufacturer relating to the selected drug as of September 1, 2023”⁹² be submitted. BMS believes that any request for patent information should be limited to information that pertains to U.S patents or applications submitted, licensed, and/or acquired directly by the Primary Manufacturer that claim or cover the selected drug as it is currently used in the commercial product. BMS requests that CMS clarify the intended meaning of “related to” and “sponsor” as the terminology seems too broad. For example, if a Primary Manufacturer provides a drug to be used by a third party in a clinical trial, and that third party files a patent application, the Primary Manufacturer might not have knowledge of such patent application or any rights to it. Additionally, BMS recommends that the Agency remove “expired” approved patents as this does not pertain to the selected drug.

Similarly, BMS requests further clarification on “patents linked to the selected drug where the Primary Manufacturer is not listed as the assignee/applicant....”⁹³ BMS believes that, as currently drafted, this request is too broad. First, the meaning of “linked to” is unclear. Second, this request would place a burden on manufacturers to search the public domain for any patent (U.S. or foreign) that may relate to the drug owned by third parties who have no relation to the Primary Manufacturer—and not to mention, something on which the Primary Manufacturer would not be fully knowledgeable. We ask CMS to remove patent reporting requirements for patents or patent applications that are not directly tied to the Primary Manufacturer as this information is not relevant for establishing the MFP and can also be compiled from the public domain without the added burden on manufacturers. If maintained, this request should be limited to U.S. patents.

With respect to exclusivity, BMS has concerns with CMS’ proposal to require reporting of “Reference Product Exclusivity for Biological Products.”⁹⁴ BMS recommends removing the associated reporting requirements, as this data element

⁹⁰ *Id.* at 87.

⁹¹ *Id.* at 53.

⁹² *Id.* at 88.

⁹³ *Id.*

⁹⁴ *Id.* at 89.

should not be provided unless the FDA has made an affirmative determination that the product is entitled to an exclusivity period. Currently, as BMS understands the process, the FDA does not make this determination at the time the biologic is first approved and only makes this determination if there is a regulatory necessity.

(d) Prior Federal Financial Support

BMS believes that the only prior federal financial support that should be reported is funding that directly resulted in a patent application containing a Government Interest Statement and/or research where a patent assignee was a U.S. government agency.

(e) Market Data and Revenue and Sales Volume Data

BMS is concerned with how vague CMS' phrasing of timeframes is throughout the Guidance, and particularly so in the "Market Data and Revenue and Sales Volume Date" section. BMS believes that the lack of consistency, coupled with broad time ranges, could inadvertently lead to discrepancies in data reporting. To minimize potential errors and create a more efficient reporting system, BMS urges CMS to consider revising its proposal to provide firm dates. For instance, CMS should clarify the definition for the "quarterly total U.S. unit volume,"⁹⁵ and provide a specific quarter on which the manufacturer to report, including which specific quarter in the past five years. Furthermore, as noted elsewhere, we assert that "lifetime" data is too broad, not relevant, and could result in inefficiencies for the manufacturer and for CMS. Finally, BMS seeks clarification on CMS' definition of net revenue—specifically what is meant by "free contingent on a purchase agreement."⁹⁶

BMS appreciates the opportunity to comment on the Guidance. We would be pleased to discuss these comments in further detail. Should you have any questions or concerns, please contact Caroline Tucker, Director, Executive Branch Strategy, at caroline.tucker@bms.com.

Sincerely,

/s/

Amy Demske
Executive Director, U.S. Policy and Executive Branch
U.S. Policy & Government Affairs

⁹⁵ *Id.* at 91.

⁹⁶ *Id.*

April 12, 2023

Meena Seshamani, MD, PhD
Deputy Administrator
Centers for Medicare & Medicaid Services
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Re: Comments on *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026*

Dear Dr. Seshamani:

California Life Sciences (CLS) appreciates the opportunity to comment on the recent guidance by the Centers for Medicare and Medicaid Services (CMS), the *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026*. As President & CEO of CLS, I welcome the chance to provide feedback on the implementation of the *Inflation Reduction Act* (IRA) and to highlight policies we believe are critical to consider when implementing this new law. While I thank you for your continued engagement with CLS, we remain concerned about the effects of this law on California's life science ecosystem and our companies' abilities to bring new, lifesaving medicine to patients.

CLS is proud to represent almost 1,200 companies and organizations across California and to advocate for the whole breadth of our state's life sciences sector, with a membership spanning biotechnology, biopharmaceutical, medical device and technology, and diagnostic companies, venture capital firms, and research hospitals and universities. California's life sciences industry generates more than 1.1 million direct and indirect jobs¹ and over \$191 billion in annual revenue², and there are more than 1,300 therapies in the development pipeline³. Maintaining a robust life science ecosystem benefits patients nationally.

The process of therapeutic development is a high risk and long-term prospect. Life sciences leaders are inspired to take on this challenge by their desire to improve the lives and health of patients and their community. CLS strongly supports policies that ensure that these products are affordable and accessible to all Americans. CLS believes that, in implementing this law, policymakers can focus on ensuring Medicare beneficiaries benefit from reduced cost sharing and broader access, while also protecting the robust life sciences ecosystem in the United States that holds the promise of new breakthrough medicines for current patients and future generations.

General overview

How CMS implements this new law will have serious repercussions for the entire life science ecosystem and will affect the innovation of medicine, with ramifications well beyond the drugs that are selected for negotiation. Decisions by CMS will have long reaching effects into future investment in small molecules, orphan conditions, and biosimilars, just to name a few areas. To ensure that these decisions are made with a complete understanding of the implications and repercussions, CLS believes a robust stakeholder process will most effectively inform the

¹ <https://www.califesciences.org/california-life-sciences-sector-report/>

² <https://business.ca.gov/industries/biotech/#citations>

³ <https://business.ca.gov/pdustries/biotech/#citations>

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agency's key decision points. To that end, CLS encourages CMS to continue to convene stakeholder panels to provide information, feedback, and help inform these decisions. CMS should systematize ongoing opportunities for patients and stakeholders to provide meaningful feedback on the agency's analyses and on the observed impact of the negotiation program's implementation. Particularly in discussions that involve therapeutic alternatives and therapeutic benefit to patients and society, patient voices are critical to understanding the real-world implications of these policy decisions.

CMS should engage with patient groups, physician groups, and other stakeholders in a more robust, open exchange without the rigidity of Information Collection Requests (ICR). CMS must proactively engage these stakeholders rather than hope for comments through ICRs. CMS's decisions will acutely affect those groups with fewer resources to expend on this process, and without more flexibility and engagement from the agency, the agency's decision will be suboptimal.

Maximum Fair Price (MFP) Considerations

The IRA statute directs the Secretary to develop and use "a consistent methodology and process that aims to achieve the lowest [MFP] for each selected drug," which must include consideration of certain specified manufacturer-specific factors, including research and development, distribution, factors related to therapeutic alternatives, and the statutory ceiling prices. As CMS works to establish this methodology, we believe the agency must create a process that maintains incentives to invest in innovations that can deliver meaningful benefits to patients as well as lower costs to beneficiaries. The process for setting the ceiling price and MFP can have significant impact on the investment in future therapeutic research and development, and CLS encourages CMS to consider the importance of driving value for patients in limiting the negotiation program's impact on the sector. Additionally, a drug should be valued for its elements over the lifetime of its use, rather than at the moment of time in the CMS offers the MFP.

To encourage innovation that benefits the patients most in need of treatment, CLS encourages CMS to establish MFPs at the ceiling price for selected products that address unmet needs or significantly advance patient care. CLS also encourages the agency to only consider manufacturer-specific data in cases where the product is held to provide fewer benefits than therapeutic alternatives.

We also believe that CMS should ensure an inclusive definition of costs – for example, research and development costs should include research costs of failures where a drug did not come to market, the cost of ongoing studies, acquisition costs for both marketed and failed drug candidates, and partnering and licensing agreements. Implementing an MFP that is reflective of the complete costs of bringing a product to market will be critical to ensure companies have the ability to continue to invest in new innovation.

As the top ranked state in National Institutes of Health funding, CLS is also concerned about the requirement for CMS to consider the use of prior federal funding in the calculation of MFP. If this could further lower the price ceiling, it may discourage the use of federal funds for drug research moving forward, and, critically for small and emerging companies, cause hesitation to invest in companies that have used such funds, particularly as there is a lack of clarity in what constitutes prior financial support. We urge CMS to ensure a balanced approach to including the use of federal funds that will not undermine the future of public-private partnerships. Additionally, we also believe CMS's suggestion that tax credits should be included goes against their intended purpose of advancing innovation in medicine and seems punitive, particularly for small and emerging companies.

Negotiation Process and Submission and Use of Manufacturer Data

CLS remains concerned about the extremely tight timeframe of 30 days that manufacturers have to submit all the required information to CMS. The information required by CMS is exhaustive and complex and will ultimately limit the amount of information a company is able to submit. We would request that CMS allow manufacturers to have a rolling data submission throughout the negotiation process, thus ensuring that CMS has complete information that will better inform negotiation between the manufacturers and the agency.

CMS has also proposed an abbreviated and restrictive negotiation process by setting a maximum of meetings, and only one at the request of the manufacturer. Given the importance of these negotiations and the complexity of the data, particularly for companies who are going through this process for the first time, we believe it is important to have a more flexible process.

Public trust in this program is essential to its success. CLS encourages CMS to establish robust safeguards to protect proprietary information from manufacturers. CLS also urges the agency to provide appropriate transparency into analyses and evaluations of selected medicines and to allow for stakeholder feedback on its assessments.

Orphan Drugs

CLS requests that CMS carefully consider the implementation of the negotiation program on drug development for rare and orphan conditions. The [law says](#) that CMS must exclude from negotiation a drug “for only one rare disease or condition and for which the only approved indication (or indications) is for such disease or condition” (Section 1191(e)(3)(A)). First, CLS believes that further clarification is needed around how “disease or condition” will be defined for the exemption and criteria that CMS will use to determine “conditions” from separate “indications.”

We remain concerned that the exemption for only one disease or condition could limit opportunities for additional research and development for indications to other rare and orphan diseases. As most of this work in additional therapeutic areas happens years after a drug is approved, if the drugs are no longer exempt, we are concerned that companies will no longer have the incentive or the ability to invest further in these products. Another area we believe needs clarification and consideration is when the timeline for negotiation eligibility would begin for a product that no longer qualifies for an orphan exemption. CMS’s interpretation of the statute and initial guidance indicates that the eligibility timeline would be based on the date of approval for the first approved indication, not approval for the additional indication. We believe that CMS should clarify that the negotiation clock only begins for an orphan drug upon approval for another condition, which will preserve researchers’ ability to pursue orphan drug candidates and continue ongoing innovations with existing drugs.

Generic and Biosimilar Markets

A robust market for generic and biosimilar drugs provides patients, Medicare, and other payers with significant savings, while encouraging ongoing therapeutic innovation. Safeguarding the incentives for generic and biosimilar development is vital for CMS to maintain long-term savings for the Medicare program and for the health care system generally. To that end, CLS encourages CMS to clarify that a selected drug will be removed from the negotiation program if a generic or biosimilar launches after the negotiation period but before the Initial Price Applicability Year begins. CLS also encourages CMS to not implement a robust and meaningful competition standard, since the *Inflation Reduction Act* statute specifically defines a qualifying single source drug as one without a marketed generic or biosimilar competitor.

Small Biotech Drug Exemption

In recognition of the potential hardships to small and emerging companies who likely do not have significant reserves or multiple products on the market or in the pipeline, the IRA exempted small biotech drugs from negotiation until 2029. However, it is critical that CMS implement this Small Biotech Exemption (SBE) in a way that is workable for the small companies it was created to support.

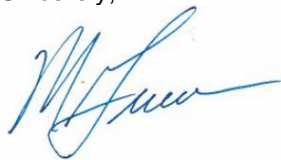
First, we believe it is imperative that CMS implement a predictable and transparent process for small biotech manufacturers applying for this exemption. This includes a clear process for how to apply for an exemption, appropriate timelines to submit information, consistent criteria for evaluating submissions, timely and clear notification if a drug meets or does not meet the SBE requirements, and a transparent dispute process for an appeal of the decision.

Second, given that this is an exemption for small biotech companies and a new program, we ask that CMS provide flexibility in its discussions with the companies and maintain a dialogue with companies throughout the process to ensure complete and accurate data submissions. Additionally, if a drug has received an SBE, and the manufacturer's circumstances have not changed in a material way, the manufacturer should not have to re-apply in subsequent years. We also believe that CMS must protect the confidentiality of the proprietary information that is submitted by a manufacturer. We support a published list of drugs that receive the SBE, but any additional information should only be released by the manufacturer, if they decide to do so.

Finally, CLS believes CMS should include a definition for what it means to be "acquired" pursuant to Sec. 1192(d)(2)(B)(ii). We believe that CMS should define an acquisition as the transfer of substantially all assets of the manufacturer. CMS should also specify whether then an acquiring manufacturer will be determined at the time of acquisition, and the acquisition results in a change in eligibility for the SBE, then an updated form should be submitted.

Thank you again for the opportunity to comment on this guidance. CLS welcomes further discussion of our comments and will happily answer any questions.

Sincerely,



Mike Guerra
President & CEO
California Life Sciences



California Public Employees' Retirement System

Executive Office

400 Q Street, Sacramento, CA 95811 | Phone: (916) 795-3829 | Fax: (916) 795-3410

888 CalPERS (or 888-225-7377) | TTY: (877) 249-7442 | www.calpers.ca.gov

April 14, 2023

Meena Seshamani, M.D., PhD, Deputy Administrator and Director
Centers for Medicare & Medicaid Services
Department of Health & Human Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850
IRAREbateandNegotiation@cms.hhs.gov

Subject: Medicare Drug Price Negotiation Program Guidance

Dear Deputy Administrator Seshamani,

On behalf of the 1.5 million active members, retirees, and their dependents that the California Public Employees' Retirement System (CalPERS) represents, we thank you for the opportunity to provide comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198. CalPERS applauds the administration's efforts under the Inflation Reduction Act to negotiate directly with drug manufacturers to lower the price of some of the costliest Medicare Part D, and eventually Part B, medications. Medicare is the backbone of CalPERS' retiree health benefits, so we appreciate your ongoing efforts to protect the long-term health of the Medicare Trust Fund and ensuring that our Medicare members will pay lower costs for these medically necessary drugs.

CalPERS is the largest purchaser of public employee health benefits in California and the second largest purchaser in the nation after the federal government. Our high-quality, comprehensive health plan offerings include health maintenance, preferred provider, and exclusive provider organization (HMO, PPO, and EPO) plans. In 2021, CalPERS spent an estimated \$10.2 billion purchasing health benefits for our members and employers. Of that, \$2.3 billion, approximately 23% of our total health care spend, was spent on pharmacy benefits post rebates, including \$934 million on Medicare members, with \$369 million of that coming from CMS Part D subsidies and \$574 million paid by CalPERS. While Medicare members only make up approximately 22% of our entire membership, they account for close to half of CalPERS overall pharmacy spend.

To provide these high-quality offerings, CalPERS relies on Medicare Advantage plans, and especially Employer Group Waiver Plans (EGWPs), because they offer enhanced value-based benefits at a lower premium than traditional Medicare. Our members include California's active and retired state and local government, school employees, and their family members, most of whom have fixed incomes.

CalPERS fully supports the elements outlined in the Medicare Drug Price Negotiation Program released March 15, 2023, particularly CMS's commitment to consider factors such as clinical benefit and unmet medical need. We also understand that CMS is not taking specific comments on Section 30 - Identification of Selected Drugs for Initial Price Applicability Year 2026 of the document. However, we have attached the top 30 most expensive Part D drugs for CalPERS Medicare population post-rebates, in case it is informative as CMS continues to refine its process for the negotiation of the Top 10 Part D drugs for 2026. We did not remove all the drugs that will be excluded from negotiation, as we thought it might be helpful to see those as well.

Thank you for the opportunity to respond to this important notice. As you move through this process, we are happy to be a resource for you, so please do not hesitate to reach out. We look forward to working with the administration to ensure the best possible options and benefits for public sector retirees.

Sincerely,

A handwritten signature in dark ink, appearing to read 'Don Moulds', with a stylized flourish at the end.

Don Moulds
Chief Health Director

Attachment

CalPERS Medicare Part D Drug Spend 2022

	Product Name	Therapeutic Level 1	Total Utilization	Total Allowed	Total Rebate Amount	Allowed less Rebate
1	ELIQUIS	ANTICOAGULANTS	80,758.00	\$80,873,078.49	\$19,422,860.82	\$61,450,217.67
2	REVLIMID*	ASSORTED CLASSES	2,282.00	\$40,249,756.40	\$50,750.00	\$40,199,006.40
3	HUMIRA PEN**^	ANALGESICS - ANTI-INFLAMMATORY	4,488.00	\$39,693,806.06	\$2,934,078.92	\$36,759,727.14
4	IBRANCE*	ANTINEOPLASTICS	2,049.00	\$30,131,247.68	\$21,396.63	\$30,109,851.05
5	JARDIANCE	ANTIDIABETICS	29,523.00	\$31,686,528.33	\$5,326,521.60	\$26,360,006.73
6	XTANDI*	ANTINEOPLASTICS	2,071.00	\$26,005,796.95	\$10,500.00	\$25,995,296.95
7	IMBRUVICA*	ANTINEOPLASTICS	1,571.00	\$23,979,256.15	\$0.00	\$23,979,256.15
8	TAGRISSO*	ANTINEOPLASTICS	1,333.00	\$23,666,541.25	\$15,750.00	\$23,650,791.25
9	XARELTO	ANTICOAGULANTS	27,988.00	\$29,821,258.78	\$7,236,065.94	\$22,585,192.84
10	TRULICITY	ANTIDIABETICS	18,081.00	\$26,180,076.81	\$4,094,970.89	\$22,085,105.92
11	OZEMPIC	ANTIDIABETICS	16,067.00	\$23,119,309.75	\$3,327,633.90	\$19,791,675.85
12	ENBREL SURECLICK**^	ANALGESICS - ANTI-INFLAMMATORY	2,529.00	\$20,290,705.27	\$1,625,070.00	\$18,665,635.27
13	PRADAXA	ANTICOAGULANTS	27,172.00	\$17,252,587.95	\$923,502.37	\$16,329,085.58
14	STELARA**^	DERMATOLOGICALS	716.00	\$16,202,059.23	\$551,780.52	\$15,650,278.71
15	JAKAFI*	ANTINEOPLASTICS	903.00	\$15,396,764.05	\$0.00	\$15,396,764.05
16	OFEV	RESPIRATORY AGENTS - MISC.	1,285.00	\$15,224,097.45	\$0.00	\$15,224,097.45
17	MYRBETRIQ	URINARY ANTISPASMODICS	24,594.00	\$20,601,960.47	\$5,561,195.99	\$15,040,764.48
18	JANUVIA	ANTIDIABETICS	17,563.00	\$19,683,867.76	\$5,095,753.57	\$14,588,114.19
19	VYNDAMAX	CARDIOVASCULAR AGENTS - MISC.	634.00	\$14,556,978.62	\$0.00	\$14,556,978.62
20	POMALYST	ANTINEOPLASTICS	653.00	\$14,533,913.85	\$0.00	\$14,533,913.85
21	DUPIXENT*	DERMATOLOGICALS	4,619.00	\$16,242,881.19	\$3,854,830.00	\$12,388,051.19
22	COSENTYX SENSOREADY PEN	DERMATOLOGICALS	2,272.00	\$13,751,701.95	\$1,365,000.00	\$12,386,701.95
23	OTEZLA*	ANALGESICS - ANTI-INFLAMMATORY	2,781.00	\$12,851,189.53	\$1,836,187.86	\$11,015,001.67
24	CALQUENCE*	ANTINEOPLASTICS	701.00	\$10,456,679.88	\$1,969.25	\$10,454,710.63
25	VICTOZA^	ANTIDIABETICS	6,693.00	\$11,586,488.64	\$1,309,776.01	\$10,276,712.63
26	ENTRESTO	CARDIOVASCULAR AGENTS - MISC.	10,704.00	\$12,142,008.44	\$2,226,974.14	\$9,915,034.30
27	SPIRIVA RESPIMAT	ANTIASTHMATIC AND BRONCHODILATOR AGENTS	16,037.00	\$10,605,789.17	\$1,189,819.30	\$9,415,969.87
28	FARXIGA	ANTIDIABETICS	10,828.00	\$11,165,544.44	\$2,588,044.51	\$8,577,499.93
29	TRELEGY ELLIPTA	ANTIASTHMATIC AND BRONCHODILATOR AGENTS	12,101.00	\$10,836,083.92	\$2,357,105.47	\$8,478,978.45
30	LANTUS SOLOSTAR^	ANTIDIABETICS	16,660.00	\$10,561,331.31	\$3,454,650.62	\$7,106,680.69

*= specialty

^ = biosimilar approved or in pipeline



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April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services
Department of Health and Human Service
200 Independence Avenue, Southwest
Washington, DC 20201

RE: Medicare Drug Price Negotiation Guidance

Dear Administrator Brooks-LaSure:

The Campaign for Sustainable Rx Pricing (CSRxP) is a nonpartisan coalition of organizations committed to fostering an informed discussion on sustainable prescription drug pricing. Our members represent organizations including consumers, hospitals, physicians, nurses, pharmacists, employers, pharmacy benefit managers and insurance providers. We are committed to developing bipartisan, market-based solutions that promote competition, transparency, and value to improve affordability while maintaining appropriate patient access to innovative prescription drugs that can improve health outcomes and save lives.

Prescription drug prices are out of control and continue to grow at unsustainable rates. Twenty-one cents of every health care dollar go toward prescription drugs – with drugs contributing more to health care costs than any other type of health care service.¹ Big Pharma increased prices on at least 350 drugs at the beginning of 2023 even though many Americans already cannot afford their needed medications.² These price increases follow years of unsustainable price increases that often greatly exceed inflation. During the period of July 2021 to July 2022, for example, drug makers raised prices in excess of inflation for 1,216 drugs, with an average price increase of 31.6 percent.³ The average price increase was nearly \$150 per drug (10.0 percent) in January 2022 and was \$250 (7.8 percent) in July 2022.⁴

Despite efforts from the pharmaceutical industry to suggest otherwise, drug manufacturers – and drug manufacturers alone – are the drivers of the unsustainable growth in prescription drug prices and the needlessly high spending on drugs that consumers, taxpayers, and businesses face today.

Drug makers set high list prices at launch and increase their prices every year they are on the market. Spending on high-priced drugs places significant strain on patients, federal health programs, and taxpayers. High-priced drugs also substantially burden the many small businesses and large employers who seek to offer affordable health insurance to their employees because, as prescription drug

¹ AHIP. “[Where Does Your Health Care Dollar Go?](#)” 2021.

² Erman M and Steenhuisen J. “[Exclusive: Drugmakers to raise prices on at least 350 drugs in U.S. in January.](#)” *Reuters*. December 30, 2022.

³ U.S. Department of Health and Human Services Assistant Secretary for Planning and Evaluation Office of Health Policy. “[Price Increases for Prescription Drugs, 2016 – 2022.](#)” September 30, 2022.

⁴ *Ibid.*



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expenditures increase, cost-sharing and premium costs also rise.⁵ Far too often patients experience the unfortunate and unfair choice of purchasing the medications they need to get well and stay healthy or paying for other necessities like food or rent. Patients simply should never be presented with such a choice.

The Inflation Reduction Act (IRA) of 2022 took major steps toward holding drug manufacturers accountable for their egregious pricing practices and the escalating costs to beneficiaries and taxpayers of unjustifiably high-priced drugs covered by Medicare. The IRA is lowering prescription drug prices for the millions of Americans who face financial uncertainty affording their medications, in part through adopting policies long advocated by CSRxP including keeping drug companies' price hikes for Medicare-covered drugs at rates below inflation and capping Part D out-of-pocket costs for beneficiaries.

CSRxP thanks CMS for efforts in soliciting public comment and input from a wide variety of stakeholders on key elements of the implementation of the Inflation Reduction Act, including the Medicare Drug Price Negotiation Guidance, and appreciates this opportunity to submit comments on this Guidance.

Indeed, pharmaceutical manufacturers already have made billions of dollars off of drugs that will be selected for negotiation in the Program, earning profits far in excess of the research and development costs they incurred to bring these drugs to market. These drug companies have set unsustainable and out-of-control prices based on "what the market will bear" with little to no consideration of what patients actually can afford. Put simply, drug manufacturers set excessively high prices for these drugs at launch many years ago and have raised those prices at unsustainable rates far in excess of inflation for years, in some cases for decades.

With this background, CSRxP respectfully offers the following comments on the Medicare Drug Price Negotiation Guidance:

1. **Identification of Qualifying Single Source Drugs Part D Drugs for Initial Price Applicability Year 2026 (30.1):** CSRxP supports the approach to treat all dosage forms and strengths of the same active moiety as a qualifying single source drug under the Program and to treat all dosage forms and strengths of a biological product with the same active ingredient as a qualifying single source drug under the Program.
2. **Negotiation Factors Regarding Therapeutic Alternatives to a Selected Drug (50):** CSRxP supports the approach to allow any interested party to submit data to CMS for the agency's consideration of evidence regarding therapeutic alternatives to drugs selected for negotiation. We agree that having access to as much information as possible will place CMS in the best position to negotiate with manufacturers the lowest possible Maximum Fair Price (MFPs) for selected drugs for negotiation.
3. **Evidence about Therapeutic Alternatives to Drugs Selected for Negotiation (50.2):** CSRxP supports the approach for CMS to consider evidence about therapeutic alternatives to drugs selected for negotiation, which includes comparative clinical effectiveness data from the selected drug's Primary Manufacturer and members of the public, including other

⁵ American Academy of Actuaries. "[Prescription Drug Spending in the U.S. Health Care System](#)." March 2018.



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manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested parties. As part of this work, we urge CMS to utilize non-discriminatory drug value assessments that will help ensure Medicare pays more for drugs that offer high value and less for drugs that do not offer the same value.

4. **Identification of Indications for the Selected Drug and Therapeutic Alternatives for Each Indication (60.3.1):** CSRxP supports the approach for CMS to identify each indication approved by the Food and Drug Administration (FDA) for a drug selected for negotiation and therapeutic alternatives for each indication. We support the use of FDA-approved indications in identifying therapeutic alternatives, as well as off-label uses of therapeutic alternatives identified in evidence-based, nationally-recognized guidelines.
5. **Starting Point for an Initial Price Offer for a Selected Drug with Therapeutic Alternative(s) (60.3.2):** CSRxP supports the proposed use of the therapeutic alternative(s)' Part D net price(s) and/or Average Sales Price (ASP)(s) as the starting point for the agency's development of the Maximum Fair Price for the selected drug unless the net price/ASP of the therapeutic alternative is greater than the statutory ceiling. This approach reflects the competitive prices generated in the market and also allows for inclusion of Part D net price(s) and/or ASP(s) of therapeutic alternatives in the development of the initial MFP offer when they otherwise may not be available. Further, in the event that there are multiple therapeutic alternatives for a selected drug, CSRxP urges CMS to use the lowest Part D net price or ASP available amongst the various therapeutic alternatives as the starting point for the initial offer.
6. **Starting Point for an Initial Offer for a Selected Drug without Therapeutic Alternative(s) (60.3.2):** CSRxP supports use of the Federal Supply Schedule (FSS) or "Big Four Agency" price as the starting point for an initial offer for a drug selected for negotiation without a therapeutic alternative or if there is a single therapeutic alternative priced above the statutory ceiling.
7. **Adjusting the Starting Point for an Initial Offer Based on Clinical Benefit (60.3.3):** CSRxP supports CMS adjusting the starting point price for the initial offer based on assessment of clinical benefit. For selected drugs with therapeutic alternative(s), we urge CMS to consider both qualitative and quantitative approaches to clinical benefit assessment where practical and appropriate in a manner that does not discriminate against the elderly, disabled, or terminally ill. For selected drugs without therapeutic alternatives, we support the approach to consider the unmet medical need of the population the selected drug is intended to treat.
8. **Consideration of Manufacturer-Specific Data in CMS' Development of a Preliminary Price (60.3.4):** CSRxP particularly supports the approach to compare the research and development (R&D) costs to the global, net revenue reported by the Primary Manufacturer to determine the extent to which the Primary Manufacturer has recouped its R&D costs. We also strongly support the agency's approach to consider the extent to which the Primary Manufacturer benefitted from Federal financial support when developing the preliminary price for the selected drug, which is consistent with statute. We recommend that CMS establish a clear process for validating the accuracy and completeness of manufacturer-submitted data.



9. **Public Explanation of the Maximum Fair Price (60.6):** CSRxP supports the inclusion of the information CMS intends to make public with respect to the process and data used to support the development of the MFP. CSRxP respectfully urges CMS to provide as much information as possible in the public explanation of the MFP. The more transparency that CMS can provide over the process and price, the greater the confidence the public and stakeholders will have that the Maximum Fair Price represents the lowest possible price the agency can justify.
10. **Monitoring for Bona Fide Marketing of a Generic or Biosimilar Product (90.4):** To protect against gaming by brand manufacturers, CSRxP supports close monitoring by CMS to determine: (1) whether a manufacturer(s) of a generic or biosimilar has engaged in “bona fide” marketing of a generic or biosimilar product that can provide competition to the selected drug; and (2) whether “robust and meaningful competition exists” if CMS indeed determines that the introduction of generic drug or biosimilar product in the marketplace has made a selected drug no longer eligible for negotiation.
11. **Part D Formulary Inclusion of Selected Drugs (110):** CSRxP urges CMS to clarify that while plans are required to cover selected drugs subject to the Drug Negotiation Program, they are not obligated to treat those selected drugs as preferred drugs and are still allowed to employ formulary tiering and utilization management tools, while at the same time ensuring that meaningful, appropriate beneficiary protections are in place.

CSRxP’s comments of the Medicare Drug Price Negotiation Program Guidance reflect our strong desire to continue working with CMS to improve prescription drug affordability while at the same time preserve access to innovative therapies that enable patients to get well and stay healthy. Without major actions, Medicare beneficiaries and taxpayers will continue to face unsustainable growth in drug prices and spending.

1. Identification of Qualifying Single Source Drugs Part D Drugs for Initial Price Applicability Year 2026 (30.1)

CSRxP supports the agency's approach to treat as a qualifying single source drug under the Program all dosage forms and strengths of the same active moiety and the same holder of a New Drug Application (NDA), inclusive of products that are marketed pursuant to different NDAs. Similarly, CSRxP supports the approach of treating all dosage forms and strengths of a biological product with the same active ingredient and the same holder of a Biologics License Application (BLA), inclusive of products that are marketed pursuant to different BLAs, as a single drug under the Program.

This approach to identifying qualifying single source drugs eligible for negotiation under the Program meaningfully helps minimize the chances of manufacturers gaming the negotiation process and finding inappropriate ways to exclude from the Program drugs that otherwise would be eligible. As a result, this approach best ensures Medicare beneficiaries can fully benefit from access to the negotiated Maximum Fair Price of the drug regardless of strength, dosage form, branding, or indications. Further, we do not anticipate that this approach will discourage innovation. Given the size of the Medicare patient population, we expect that manufacturers have sufficient incentives to engage in research and development of new therapies and new indications of existing therapies, leading to future innovations in treatment.

2. Negotiation Factors Regarding Therapeutic Alternatives to Drugs Selected for Negotiation (50)

CSRxP supports the approach to allow any interested party to submit data and evidence to CMS about therapeutic alternatives to drugs selected for negotiation as negotiation factors for consideration. Information and evidence from members of the public, including manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested parties will meaningfully help to inform the agency's negotiating position. With access to as much information as possible, CMS will be in the best position to negotiate effectively to arrive at the lowest possible Maximum Fair Price for selected drugs.

3. Evidence About Therapeutic Alternatives to the Selected Drugs (50.2)

CSRxP supports the approach that CMS to review and assess comparative clinical effectiveness research about therapeutic alternative(s) to the selected drug as part of the agency's work in developing an initial price offer to the selected drug's Primary Manufacturer. Having access to comparative clinical effectiveness data from the Primary Manufacturer and members of the public, including other manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested will give CMS important evidence and data to make an informed initial price offer that ultimately aimed to result in the lowest possible Maximum Fair Price for the selected drug under negotiation in the Program.

As part of this overall work, CSRxP particularly urges CMS to review drug value assessments submitted by interested parties. Use of drug value assessments that incorporate both clinical evidence and cost will best ensure that Medicare pays pay more for drugs that offer high value to Medicare beneficiaries and less for drugs that do not offer that same level of value to beneficiaries. Consistent with requirements in the IRA, we agree and believe that assessments CMS considers as part of this overall



process should reflect the rights and needs of all Medicare beneficiaries and must not discriminate against the disabled, elderly, or terminally ill. However, CSRxP believes there are health measures that do not violate the IRA statutory prohibition; these non-discriminatory drug value assessments are an extremely valuable source of information and CSRxP strongly supports using as much of such research as possible in the negotiation process. Further, CSRxP strongly supports the agency's intent to consider studies that clearly separate prohibited evidence from other evidence that this relevant to the negotiation process.

4. Identification of Indications for Selected Drugs and Therapeutic Alternatives for Each Indication (60.3.1)

CSRxP supports the proposal for CMS to identify each FDA-approved indication for a drug selected for negotiation under the Program and for CMS to identify therapeutic alternative(s) for each indication of the selected drug. We strongly support the notion that indications of therapeutic alternative(s) for comparison should include both FDA-approved indications *and* off-label uses of drugs identified in evidence-based, nationally-recognized guidelines as therapeutic alternative(s). By including both on-label and off-label indications in the scope of therapeutic alternative(s) to the drug selected for negotiation, CMS will have a greater number of comparators to use in the development of the lowest possible Maximum Fair Price that the agency can justify.

5. Starting Point for CMS' Initial Price Offer for a Selected Drug with Therapeutic Alternative(s) (60.3.2)

CSRxP supports use of a therapeutic alternative(s)' Part D net price(s) and/or ASPs as the starting point for the development of the Maximum Fair Price for a selected drug – unless the net price/ASP of the therapeutic alternative is greater than the statutory ceiling. This approach importantly reflects the competitive prices generated in the marketplace and also allows for inclusion of Part D net price(s) and/or ASP(s) of therapeutic alternatives in the development of the initial MFP offer; other approaches under consideration by CMS would not necessarily allow for the inclusion of potentially lower net prices and/or ASPs of therapeutic alternatives in the development of the initial price offer.

Furthermore, in the event that there are multiple therapeutic alternatives for a selected drug, CSRxP urges CMS to use the lowest Part D net price or ASP available amongst the various therapeutic alternatives to serve as the starting point for the initial offer. Utilization of the lowest Part D net price or ASP of all possible therapeutic alternatives as the starting point for the initial offer importantly will best ensure that the ultimate Maximum Fair Price represent the lowest possible price CMS can justify for a drug selected for negotiation.

6. Starting Point for CMS' Initial Offer for a Selected Drug without Therapeutic Alternative(s) (60.3.2)

CSRxP supports the use of the Federal Supply Schedule (FSS) or "Big Four Agency" price as the starting point for an initial offer for a drug selected for negotiation without a therapeutic alternative. CSRxP also supports use of the FSS or "Big Four Agency" price in the case where there is a single therapeutic alternative priced above the statutory ceiling. Both pricing approaches – the FSS and "Big Four Agency" price – reflect prices negotiated by the federal government for other federal health programs and

therefore represent appropriate starting points for CMS' development of an initial offer for a selected drug without therapeutic alternatives.

7. Adjusting the Starting Point for an Initial Offer Based on Clinical Benefit (60.3.3)

CSRxP supports CMS adjusting the starting point for the initial price offer of selected drugs with therapeutic alternative(s) based on assessment of clinical benefit. Without reflecting relative clinical benefit, the Maximum Fair Price will not reflect the value of the selected drug to Medicare beneficiaries and subpopulations of interest.

Further, CSRxP recognizes that CMS wants to preserve flexibility in adjusting the starting point for the initial offer based on clinical benefit by using a qualitative approach to such adjustment. We appreciate that nuanced differences exist amongst different therapeutic options that CMS should consider as it determines potential adjustments to the initial price offer. However, CSRxP respectfully recommends that CMS also employ a quantitative approach to the extent possible and appropriate when making adjustments to the initial price offer based on clinical benefit. Quantitative approaches that appropriately consider value without discriminating against the elderly, terminally ill, and disabled can help CMS ultimately to arrive at the lowest possible Maximum Fair Price the agency can justify.

Additionally, for selected drugs without therapeutic alternatives, CSRxP supports the approach to consider the unmet medical need of the population the selected drug is intended to treat. Patients with unmet medical needs meaningfully benefit from access to treatments and therapies that can improve their overall health and well-being.

8. Consideration of Manufacturer-Specific Data in CMS' Development of a Preliminary Price (60.3.4)

CSRxP supports the overall process CMS outlines in the Guidance for consideration of the Primary Manufacturer's submitted data in developing the preliminary price for the selected drug. The process described generally aligns with statutory requirements. In particular, CSRxP strongly supports the agency's preferred approach to compare the Primary Manufacturer's R&D costs to its reported global, net revenue in order to determine the extent to which the Manufacturer has recouped its R&D costs. Use of global sales, rather than only U.S. sales, appropriately reflects the actual profit to the Manufacturer of developing, marketing, and selling the drug over time.

CSRxP also strongly supports the agency's approach to consider the extent to which the Primary Manufacturer benefitted from Federal financial support when developing the preliminary price for the selected drug. Section 1194(e) of the IRA specifically directs the HHS Secretary to consider factors from manufacturer-submitted data on "[p]rior Federal support for novel therapeutic discovery and development with respect to the drug."⁶

Further, to ensure data submitted by Primary Manufacturers are accurate and complete as possible, CSRxP strongly encourages CMS to develop a stringent process for validating Manufacturer-submitted data used in price negotiations. A clearly established data process will best ensure that CMS has the most complete and accurate information available as it engages in negotiations with manufacturers to

⁶ IRA Section 1194(e)(1)(C)



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reach the lowest possible Maximum Fair Price for a selected drug that the agency can justify. Additionally, as CMS evaluates ways to ensure the long-term success of the Negotiation Program, we recommend considering research and partnership with external stakeholders to gather unbiased data on manufacturer R&D costs that can help validate the accuracy and completeness of the data submitted by Manufacturers and help inform the negotiation process in future years.

Finally, while it is helpful to have information on the Primary Manufacturer's R&D costs, CSRxP recommends that CMS should exercise caution in attributing significant weight in negotiations process to this information given the lack of external, non-biased resources to help verify manufacturer R&D cost data – even with a data validation process in place as suggest. We strongly believe that CMS should place greater weight on other data, primarily drug value assessments that provide information on the clinical benefit and cost of therapeutic alternatives. In so doing, CMS will best ensure that the Maximum Fair Price represents the lowest possible price that can be attained for Medicare beneficiaries and taxpayers.

9. Public Explanation of the Maximum Fair Price (60.6)

The Guidance states that CMS intends to publish on its website:

- the selected drug, the initial price applicability year,
- the MFP file (which would be updated annually to show the inflation-adjusted MFP for a selected drug),
- and the explanation for the MFP, including a summary of how relevant negotiation factors were considered during the negotiation process and those that had the greatest influence on determining the MFP, among other information.

CSRxP appreciates and supports all of the information CMS intends to make available to the public regarding the Maximum Fair Price for a drug selected for negotiation under the Program. To the maximum extent possible, we respectfully urge CMS to provide as much information as possible to the public. With a high level of transparency, Medicare beneficiaries, taxpayers, and other stakeholders will have appropriate confidence that the Maximum Fair Price amount represents the lowest possible price CMS can justify for a selected drug.

10. Monitoring for Bona Fide Marketing of a Generic or Biosimilar Product (90.4)

The IRA requires CMS to remove a selected drug from negotiation eligibility in the Program if that drug becomes subject to competition from either a generic drug or biosimilar biological product. CSRxP strongly supports the agency's approach to closely monitor whether or not the selected drug actually faces competition and thus no longer is eligible for, or subject to, negotiation under the Program. We specifically support the overall process for CMS to determine: (1) whether a generic and/or biosimilar manufacturer(s) has engaged in "bona fide" marketing of a generic drug or biosimilar biological product that can provide competition to the selected drug; and (2) whether "robust and meaningful competition exists" if CMS indeed determines that the introduction of generic drug or biosimilar product in the marketplace has made a selected drug no longer eligible for negotiation. CMS' monitoring approach will help protect against gaming by manufacturers of drugs that otherwise should be eligible for negotiation.

11. Part D Formulary Inclusion of Selected Drugs (110)



the campaign for **SUSTAINABLE Rx PRICING**

CSRxP urges CMS to clarify that, while plans are required to cover selected drugs subject to the Drug Negotiation Program, they are not obligated to treat those selected drugs as preferred drugs and are still allowed to employ formulary tiering and other utilization management tools. Maintaining the ability to use these tools will best ensure that plans can negotiate effectively with pharmaceutical companies to lower overall prescription drug costs and spending for Medicare beneficiaries and taxpayers, while at the same time ensuring that meaningful, appropriate beneficiary protections are in place.

Conclusion

In conclusion, CSRxP again wishes to thank CMS for the opportunity to comment on the Medicare Drug Price Negotiation Guidance. Prescription drug prices are out-of-control and are only getting higher. Medicare beneficiaries and taxpayers simply cannot continue to pay for needlessly high-priced drugs that increase the profitability of Big Pharma at the expense of patients and taxpayers. CSRxP looks forward to our continued work with the Administration to make prescription drugs more affordable for all American patients and their families while at the same time maintaining access to the treatments that can improve health outcomes and save lives.

Sincerely,

Lauren Aronson
Executive Director
Campaign for Sustainable Rx Pricing

CANCER LEADERSHIP COUNCIL

A PATIENT-CENTERED FORUM OF NATIONAL ADVOCACY ORGANIZATIONS
ADDRESSING PUBLIC POLICY ISSUES IN CANCER

April 14, 2023

Meena Seshamani, MD, PhD
Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Filed electronically at IRAREbateandNegotiation@cms.hhs.gov

Dear Deputy Administrator Seshamani:

The undersigned organizations representing cancer patients, health care professionals, researchers, and caregivers appreciate the opportunity to comment on the Initial Memorandum for Implementation of the Medicare Drug Price Negotiation Program. The negotiation of drug prices may have substantial effects on cancer patients, and we offer advice below regarding actions that the Centers for Medicare & Medicaid Services (CMS) can take to ensure that the advice of cancer patients, cancer care providers, and other cancer stakeholders is obtained and fully considered during the negotiation process.

For cancer patients and their cancer care teams and families, a cancer diagnosis begins a complex and difficult journey. Many cancer patients have benefited greatly from advances in screening, diagnosis, and treatment advances, and as a result the cancer journey is a long one. For some, the journey ends in cure and for others a good life even without a cure.¹ Cancer patients often find treatment a complicated process, with the need to manage not only their treatment but also the side effects of cancer and cancer treatment, including physical symptoms, psychosocial issues, employment issues, and financial toxicities. Cancer patients, even when faced with a life-changing diagnosis, are required to plan and manage their care and their lives. All too often, they become expert at addressing both expected and “unintended” consequences of cancer and cancer treatment.

¹ The cancer death rate has declined by 33 percent since 1991, due to treatment and screening advances and less smoking. Siegel, et al. Cancer Statistics, 2023. CA: A Cancer Journal for Clinicians. January 12, 2023.

Cancer survivors and cancer advocates, because of their cancer experiences, are well-qualified to offer advice about the drug price negotiation process and to recommend options for monitoring the possible unintended consequences of price negotiation.

Input Regarding Clinical Benefit

In the guidance document, CMS generally describes a process through which it will seek information about the clinical effectiveness of a selected drug and the drug's therapeutic alternatives. Cancer patients are, as we describe above, well-prepared to offer advice about clinical effectiveness of selected drugs. CMS notes that it is interested in real-world evidence about selected drugs, and cancer patients can supply that evidence, including about drugs' side effects and tolerability. They can offer detailed real-world perspectives on selected drugs and therapeutic alternatives. In these comments we focus on the input of cancer survivors but believe that health care professionals, including those involved in the development of evidence-based practice guidelines, should be part of the process for evaluating clinical benefit and comparing therapeutic alternatives.

In recent years, the Center for Medicare & Medicaid Innovation (CMMI) at CMS has sought and received the advice of cancer patient advocates related to alternative payment and delivery models, including the Oncology Cancer Model and the Enhancing Oncology Model. Patient advocates have found CMMI open and transparent in the consultation process, in some circumstances agreeing to attend meetings convened by advocacy organizations to receive those advocates' advice.

We urge that a process or procedures be established to solicit the advice of patients about selected drugs and that the advice be solicited and evaluated in timely fashion. Some have suggested that there be something akin to an ombudsman as the central point for engagement with patients, with the Patient Affairs Office at the Food and Drug Administration cited as a model. Others have suggested a standing panel of patient stakeholders to be consulted by CMS. We do not reject these suggestions but are concerned that these structures or processes may not result in timely advice from patients, which we define as advice about clinical benefit and therapeutic alternatives during the negotiation process.

We want to avoid a situation where patients provide valuable advice about clinical benefit, but that advice is received at the end of the negotiation process, essentially serving as commentary on a completed process. Even when federal agencies have good intentions regarding patient input, they sometimes solicit and receive that advice "after the fact" of a dynamic public policy process.

Public notice to patient advocates about an ongoing negotiation process, alerting them to a meeting to discuss a selected drug and an opportunity to submit written comments, might be an efficient way to obtain patient advice. Because the price negotiation process is being implemented through sub-regulatory guidance, the agency has some flexibility regarding notice

and invitation to advocates and convening of panel meetings and acceptance of advice. The insights of patients are critical to the drug price negotiation process, and we look forward to flexibility and transparency from CMS in how it seeks and evaluates that research. CMS states in the initial guidance that the statute, “requires that CMS not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.” We appreciate that CMS has, throughout the initial guidance, underscored the statutory limits on the use of QALYs and its intention to honor those limits.

Unintended Consequences of Drug Price Negotiation

As we have noted above, many cancer survivors have benefited tremendously from cancer research advances. When we talk about the expertise of cancer survivors across the continuum of care, that encompasses expertise about research and development of new therapies. Advocates are quite sophisticated about the drug development pipeline and will be monitoring the possible impact of drug price negotiation on investment in research and development. We urge CMS to regularize and formalize its efforts to ascertain the potential unintended consequences of price negotiation.

Pharmaceutical company representatives are raising alarms to patient advocates that their investment in research on supplemental indications of approved drugs will be significantly adversely affected by the price negotiation process. We are concerned about this assertion from the pharmaceutical industry, and research on supplemental indications will be among those research endeavors that the advocacy community will closely monitor.

Additional Efforts to Address Affordability of Drugs

We end our comments with observations and advice about other drug affordability issues. We realize that the issue of advice regarding the implementation of the “smoothing” of beneficiary cost-sharing responsibilities is outside the scope of this guidance. However, this issue is critically important to patients, and we look forward to implementation decisions regarding smoothing soon.

Clearly outside the scope of this guidance are additional efforts to address the affordability of drugs, including insurance reforms and limits on utilization efforts. We will pursue such reforms, as they are a critical complement to any relief that patients may see from drug price negotiation. We simply want to acknowledge that, whatever benefits are realized from drug

price negotiation, they will not fully address the drug affordability issues that are crippling for some cancer patients.

We appreciate the opportunity to offer our input regarding the drug price negotiation initial guidance.

Sincerely,

Cancer Leadership Council

Association for Clinical Oncology
CancerCare
Cancer Support Community
Children's Cancer Cause
Fight Colorectal Cancer
LUNgevity Foundation
Lymphoma Research Foundation
National Coalition for Cancer Survivorship
Ovarian Cancer Research Alliance
Susan G. Komen

CareSet Comments on the Medicare Drug Price Negotiation Program Initial Guidance

These comments are in response to the guidance found here:

<https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>

Under the Inflation Reduction Act (IRA), Centers for Medicare and Medicaid Services (CMS) will negotiate fair pricing for high-cost medications. CMS will also have to decide which data and evidence it receives from drug manufacturers during this negotiation process will be released to the public.

This negotiation must balance two opposing goals. First, Medicare beneficiaries deserve to pay reasonable prices for the medications they need, and second, pharmaceutical companies must be allowed to sustain profits that justify access to the financial capital they need to create new medications. This policy balance is embodied within the law with the concept of the Maximum Fair Price (MFP).

CareSet is a healthcare research and data journalism organization, as well as a data vendor. There are two general categories of interest to CareSet within this guidance.

- What information should be considered proprietary?
- What types of evidence should CMS accept when it evaluates the performance of medications?

Achieving the right balance on these issues will allow researchers, journalists, and members of the public to measure the effectiveness of the law, related regulations and guidance, and the government's performance in negotiating lower medication costs.

What information should be considered proprietary?

CMS will publish portions of the information that was submitted by the pharmaceutical company as part of the negotiation process. CMS has requested feedback regarding what information should be regarded as proprietary to avoid “treating information that does not qualify for such protection as proprietary.”

CMS has also requested feedback on what components of the negotiation process itself should be private and the degree to which that privacy should be permanent.

The IRA instructs the Secretary to determine what information will be considered proprietary [42

[U.S.C 1320f-2\(c\)](#)].

CMS has a responsibility to demonstrate the effectiveness of its IRA implementation

The central mandate from Congress to CMS is to create “a consistent methodology and process” that achieves “the lowest maximum fair price for each selected drug”.

FOIA exists to inform the public about the actions of its government and to provide citizens with political choices. It mandates the release of materials that are “likely to add to the fund of information that citizens may use in making vital political choices”. Given the unprecedented nature and political controversy of the IRA, the public being informed of the success of the IRA and its implementation will likely be of great importance to FOIA courts.

CMS must not create a commitment to the industry that data will be proprietary

CMS should not embed any specific promises, in regulation, that certain information is proprietary to medication manufacturers. Doing so creates an expectation that an exemption to FOIA should apply where none is warranted and means that information might be permanently withheld from public scrutiny. It should be the responsibility of the drug manufacturers to assert what should be private and then CMS should evaluate those assertions. There is no reason for CMS to proactively protect any specific information by making promises in regulation that will be enforced even after they have become out-of-date.

FOIA Exemption 4 governs evaluation of the proprietary status of information submitted to the government.

The first component of evaluating whether information is proprietary under Exemption 4, post-*Argus*, considers whether data is “customarily kept private, or at least closely held”.

The second component is whether the government provided an assurance that information would be kept confidential.

Prices should not be proprietary

The central mission of this negotiation program is to use the volume of patients covered under Medicare to negotiate a favorable rate for the purchase of medications. It is only comparison

with the non-FAMP (i.e. the prices charged outside of Medicare) and Plan Specific Enrollment Weighted Amounts (i.e. prices charged within Medicare Part D) that allows for the public to be able to evaluate whether this program is working.

The CMS guidance only conceptualizes information as “proprietary” or “already public”. However, this ignores the “industry arcana” effect, where an industry excludes outsiders from information, while ensuring that everyone in the industry is well-informed.

Manufacturers cannot argue that prices are kept private, when an entire industry exists that relies on perfect or near-perfect knowledge of pricing. Data vendors sell medication pricing information regularly to third parties, which is how the manufacturers know what their competitors are charging for their products.

This knowledge hardly qualifies as proprietary, since at least three parties know the price of all large payor transactions, given that prices are negotiated by Pharmacy Benefit Managers (PBMs). Therefore, multiple parties are “in” on the financial details of nearly every medication price negotiation.

However, the industry still excludes Congress, researchers, and journalists from the data they need to understand if a market is functioning correctly. Given that PBMs are now connected with both pharmacies and insurance companies, this knowledge is well-disseminated. In short, the only people who are not aware of medication industry pricing are those entities that would seek to hold the medication industry accountable for those prices. CMS should never consider information that the majority of an industry knows to be “private”, and should therefore consider the wide commercial availability of data that they choose to label as “proprietary”. This principle applies centrally to prices, but is also relevant to other types of information.

A rule of thumb: if a pharmaceutical manufacturer cannot demonstrate that their “confidential” data is not well-known by their competitors, then CMS should ensure that this data is fully open to the public.

To illustrate this point - If Medicare is currently paying a manufacturer \$100 for a pill and the new negotiated MFP is \$90, this might seem like a victory for CMS. However, if the public was aware that the going rate for the medication to other payers is \$70, it would be clear that taxpayers are overpaying. Without the “going rate” information it will be impossible to tell whether CMS is actually successful in its negotiations.

If CMS is unwilling to provide this transparency, then CMS must clearly delineate the manner in which it will demonstrate to Congress and the public that its program is calculating the right price.

Process should not be entirely private

CMS asks for feedback on the currently secretive negotiation process. The process includes rounds of negotiations with evidence being passed back and forth between a manufacturer and CMS, most of which is held private until it is ultimately deleted.

We understand that at least some parts of the negotiation should be private. However, CMS should avoid policies which block transparency forever. CMS should consider methods to enable partial transparency. For instance, CMS should insist that all efficacy and cost-effectiveness research that is used by the manufacturer during the negotiation be listed publicly. CMS should publish a list of which evidence was referenced by both CMS and the manufacturer, during each step of the negotiation process, including research on medications that are in competition with the medication under negotiation.

CMS should further consider releasing the full negotiation records 5-10 years after the patent coverage for a medication expires, rather than mandating that they be destroyed.

Generally, CMS should be embracing a multi-pronged approach in protecting the vital trade secrets of manufacturers, as well as providing the marketplace with open data and evidence on whether a specific medication is worth its costs. If these suggestions are not workable, then CMS should consider other mechanisms to inform the marketplace of relevant data to ensure long-term competition to lower prices across many different medication classes and diseases.

What drug performance data should be considered as part of ongoing negotiations?

CMS will also be required to gather and evaluate evidence regarding the effectiveness of medications. CMS should accept data of various types and not only those currently in vogue for real-world evidence. This includes:

- Evidence that is not released as articles in medical journals, including alternative evidence containers such as whitepapers and data dashboards.
- Aggregated patient experiences, including those from patient data registries.

CMS evaluations of evidence (both from manufacturers and from third parties), should be fully transparent. If CMS does not think evidence is relevant, it should clearly state why for each evidence submitted. Journalists and researchers should be able to easily quantify and analyze the evidence evaluation process to determine if CMS is preferring certain types of evidence, researchers, or research approaches.



April 14, 2023

Meena Seshamani
Deputy Administrator and Director
Centers for Medicare & Medicaid
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Dear Director Seshamani,

On behalf of The Center for Medicine in the Public Interest (CMPI), I am writing in regard to the initial implementation guidance for the Inflation Reduction Act's "Medicare Drug Price Negotiation Program" for initial price applicability year 2026.

CMPI is a nonprofit, nonpartisan organization, committed to advancing the discussion and development of patient-centered health care.

Collectively, we are concerned that the Centers for Medicare and Medicaid Services (CMS) guidance could stifle medical innovation, discourage biosimilar manufacturers from entering the market, and put patients in jeopardy of losing the medicines they need.

First, the timeframe provided by CMS to respond to this initial guidance is insufficient. A thirty day-window restricts the capacity of interested stakeholders' to review the sections in question and provide meaningful input. Small life sciences companies, physicians, and patients are particularly at risk of not having their voice heard.

As for the content of the guidance, the detailed standards for price setting only compound our concerns with the statute itself.

In order to determine the maximum fair price (MFP) of a drug for the Negotiation Program, CMS plans to use therapeutic reference pricing as a guideline. Therapeutic reference pricing involves comparing a drug to a therapeutic alternative -- one that is chemically different but, in theory, provides similar clinical outcomes.

In practice, this reference pricing is arbitrary and fails to consider critical differences in patient needs and preferences. For example, if a patient is unable to receive an intravenous form of medication -- due to an immunodeficiency that leaves them susceptible to infection -- an

alternative medication that is taken in pill form may be the most effective way to treat their condition.

Using therapeutic reference pricing as the basis for MFP price-setting would result in clinically inappropriate decisions that disregard such variations in patient needs.

As part of the guidance, CMS also proposed that a decidedly narrow definition of unmet need be taken into consideration during the price-setting process. The agency's definition of unmet need is reserved for certain diseases with very limited or no alternative treatment options. CMS will "adjust the starting point for the initial offer" for drugs that meet these criteria.

This severely limited definition would undercut the value of critical medicines for a range of serious conditions that have alternate treatment options. Patients benefit from continued innovation of new therapeutics that address differences in preferences and needs. Proceeding down this path would only disincentive such innovation.

Relatedly, the price-setting guidelines CMS put forth in the guidance fail to convey how medical research and development will be protected with the proposed conditions in place. The predictable outcome of price controls is the significant disincentivization of the research and development system that makes America the world leader in medical innovation.

Developing medicines is already a risky business. It costs, [on average](#), nearly \$3 billion over 10 to 15 years for each approved new medicine. That's partly due to the direct expense of the research and development activity itself -- and partly because [only 12%](#) of potential medicines entering Phase I clinical trials ultimately win final FDA approval. Private investors are only willing to take such risks because a successful drug has the potential to make up for the cost of failures and then some.

President Biden has previously [claimed](#) that under a price control regime, "drug companies will still do very well." In fact, price controls could reduce the revenue of the innovative biopharmaceutical industry by [\\$1.5 trillion](#) over the next decade. Biopharmaceutical companies, on average, dedicate nearly one-fifth of revenue to research and development.

Simple math suggests that price controls will force innovative firms to slash R&D spending by hundreds of billions of dollars. A [past analysis](#) of a policy similar to the IRA found that price controls could lead to 56 fewer new drugs -- including 16 lost cancer treatments.

Some estimates are even more worrying. [A review](#) led by University of Chicago economist Tomas Philipson concluded that price control legislation would reduce industry revenue by 12% through 2039 and R&D activity by 18.5%, or \$663 billion. Philipson estimated the result would be 135 fewer medications being developed in that period -- a crippling shortfall that will also be measured in lives lost.

Whether the number of lost drugs is 56, 135, or somewhere in between, the reality is clear: Under CMS' new guidance, which reinforced misguided policies in the IRA, breakthroughs in cancer, Alzheimer's disease, ALS, heart disease, and many other illnesses are in serious jeopardy.

Setting artificially low prices will drive away investors, given that they will no longer have the surety of being able to recoup their innovative investments. Indeed, a recent survey revealed that almost two thirds of companies plan to shift R&D efforts away from small molecule medicines. Meanwhile 95% of the surveyed companies anticipated major cutbacks on research into new uses for their medicines given the limited time before government price setting kicks in.

CMS' guidance exacerbates this R&D concern by stating that if drugs have existing patents or exclusivities that protect their innovation "for a number of years," the agency has the right to adjust the initial offer price downward.

The proposed policy could penalize companies that obtained patent rights before FDA approval. However, it could entirely upend the pursuit of costly post-approval R&D, which often yields meaningful and inventive benefits for patients.

Consider cancer treatments, for example. Nearly 40% of Americans will be diagnosed with cancer in their lifetime. And these patients rely on post-approval R&D -- underpinned by patent and exclusivity protections -- to bring new treatment uses, formulations, dosage flexibilities, and more to the table. In fact, among oncology drugs that were granted approval a decade ago, 60% went on to receive further approvals.

As it stands, CMS' guidance could leave these patients, and countless others, worse off.

Even biosimilar manufacturers face increasing unpredictability in the wake of CMS' guidance. Per Congress, the "Special Rule," is supposed to enable manufacturers to request delayed selection for price-setting for select reference biological products.

However, the steps and criteria listed to obtain a delay in price negotiation, in addition to the timeline surrounding the process, creates further confusion. This needless uncertainty could cause biosimilar manufacturers to reconsider whether they'll enter the market.

That, in turn, could lead to a major loss in patient savings. Biosimilars are instrumental in providing cost-effective treatments to patients. According to one study, biosimilars are projected to save Americans over \$38 billion in drug costs between 2021 and 2025.

CMS' initial guidance, as well as the IRA itself, rely on a troubling misunderstanding of the drug development pipeline, and the role the federal government plays in it. Many policymakers seem to believe that pharmaceutical innovation is [primarily driven](#) by the National Institutes of Health, the federal medical research organization. But that has simply never been true.

A study in the journal *Health Affairs* by two Columbia University scholars analyzed mounds of historical data to reveal the real role the NIH serves in drug development. This study definitively [concluded](#) that fewer than 10 percent of drugs are covered by a public sector patent. And this slice of drugs only accounts for 2.5 percent of total annual drug sales. Drugs that relied on federal funds for development, meanwhile, comprise only about a quarter of sales.

In reality, the primary engine of drug innovation is private industry, which [spends tens of billions](#) of dollars annually on research and development. The NIH, while important, focuses on basic research -- that is, the study of fundamental aspects of organic phenomena without regard to specific medical applications.

The innovative private biopharmaceutical industry, on the other hand, directs most of its efforts toward practical, clinical research. These firms' work is centered on the actual development of new medicines.

Both the NIH and private firms play a role in financing the important research that happens at academic institutions. But the reality is that private industry employs most of the scientists that take part in hands-on drug development. In sum, drug development is a team effort and is too often mischaracterized by politicians, pundits, and agenda-driven advocates who aim to pit the federal government and private industry against one another.

Lastly, the new guidance seems to double-down some policymakers' misleading and inappropriate focus on a drug's "list price" while largely ignoring the pernicious market dynamics actually responsible for many access and affordability issues.

In many cases, the list price of a medicine is meaningless to patients. When Americans with health insurance say that their drugs are too expensive, what they often mean is that their copays and coinsurance rates are too high. But those rates aren't set by pharmaceutical companies. They're actually the domain of the pharmacy benefit managers and insurance companies. During the last few years, pharmaceutical spending has increased by 38% while the average individual health insurance premium has increased by 107%. During the same period, rebates, discounts, and fees paid by the biopharmaceutical industry to insurers and pharmacy benefit managers have risen from \$74 billion to \$166 billion. That's equal to 37% of our nation's entire drug spending. Government policies should encourage these rebate dollars to flow back to patients, not to the pockets of middlemen who don't invent or manufacture a single drug.

Worse still, the rebates that manufacturers pay to pharmacy benefit managers are often tied to drugs' placement on restrictive formularies. This creates a destructive incentive for entrenched middlemen to give formulary space only to the manufacturers who can offer the biggest rebates - even if such large rebates require astronomically high list prices. This perverse model, coupled with constantly escalating cost-sharing requirements, harms patients and reduces access to life-saving medicines.

Allowing pharmacy benefit managers to continue with business-as-usual makes it impossible to build a health care ecosystem based on competitive, predictable, free-market principles.

CMPI's concerns with CMS' initial guidance ultimately boil down to a responsibility we have to advocate for patient-centered health care. Given the limited window to respond to its troubling components, this guidance has the potential to disrupt future medical innovation and impede optimal patient outcomes.

We hope that you take into consideration our concerns, as well as those of other affected parties, and revise this guidance accordingly.

Thank you.

Respectfully,

Peter Pitts
President
The Center for Medicine in the Public Interest



April 11, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Cerebral Therapeutics' appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

Cerebral Therapeutics is a clinical-stage biopharmaceutical company taking forward small molecules for central nervous system, or CNS, disorders for patients and diseases with serious unmet need. The company uses its expertise in direct to CNS therapies and therapy development, including in preclinical, clinical and neuromodulation commercial execution to enable the development of medications and therapies to effectively bypass the Blood Brain Barrier. CT's approach achieves higher local doses in the brain where it is needed, lower systemic doses which avoid many systemic adverse events along with the precision medicine along with the ability to administer and sample serially safely from the CSF within the brain. CT's approach has the potential to transform critical areas of unmet need in CNS drug development.

We recognize that CMS has said they are not accepting comments, in particular regarding Section 30. Nevertheless, we are providing comments including for Section 30 as Section 30 is concerning. Our concern is that the proposed legislation will create economic conditions which will substantially limit drug development for non-biologic agents which we hope is an unintended consequence as it is likely to negatively impact our society. Please see below.

I. [Section 30.1 Comments] Considered together as a single source from a pricing perspective, a single drug for multiple individual diseases, substantially enhances the barrier to developing new therapies for patients with unmet medical needs. Given the complexity costs and timeline for each new indications the 9-year negotiation limit will essentially mean that development can only be feasible for at most one disease per molecule as development has to happen sequentially in not in parallel if one drug can be used in more than one disease because of FDA processes and cost and requirements to focus on a single indication for approval. This section of the legislation will have the consequence of drastically limiting CNS drug development for small molecules. This is deeply unfortunate as it will make many CNS diseases with unmet need we are considering

Cerebral Therapeutics, Inc.

12635 Montview Boulevard, Suite 137, Aurora, CO 80010 // 3510 Hopkins Place N, Building 4, Oakdale, MN 55128



no longer feasible. A feasible way to mitigate the harm to society is to consider the timeline for drug pricing for each disease on its own independently. The impact of this problem alone is significant but compounded with the problem in the next section is very significant.

II. [Section 30.1.1 Comments] As a developer of small molecule orphan drugs for severe CNS disease, this part of the legislation will have the result of drastically curtailing development of therapies for follow-on rare diseases. Rare diseases already struggle with funding due to low patient numbers, but this approach will make many rare disease programs unfeasible. For example, we currently are looking at bundling several rare diseases together using a single therapy that individually would not be financially feasible due to the complexity, costs and regulatory processes for therapies like ours. A feasible way for CMS to mitigate the harm is to change the timing to 13 years for the NDA path for small molecules/ non-biologics with active orphan designations. The impact of this problem alone is significant but when compounded with the problem in the previous section is very significant.

III. [Section 50.2 Comments] Cost effectiveness calculations embraced by ICER as they currently operationalize their mission underestimate the impact of meaningful human improvement from debilitating disease. This is particularly important in the CNS disorders that my company addresses as inappropriately constrained to measures of cost effectiveness are prone underestimate the value of drug therapies thereby discouraging drug development that may make a meaningful difference in patients lives with CNS disease. The proposed ICER approach could be substantially improved for companies like ours that treat complex CNS diseases by broadening ICER criterion to include value elements that more accurately reflect the true impact of the therapy rather than an narrowed consideration of patient impact which is not thoughtfully enough considered.

IV. [Section 40.2.2 Comments] As CMS is responsible for policies that are government driven and impact a broad part of the population, the CMS process for determining value should be transparent. This is critical for small drug development companies like ours which are accountable to board and investors to know that there is an open and equitable rules-based system. Furthermore, the therapies that we develop, are complex and address unmet needs for Central Nervous System Disorders are continuously being clarified and refined as science progresses. An open transparent process facilitates partnership and learning and is important to companies like ours as well as the patients we serve who may wish to help CMS understand unmet need. This relative transparency has allowed bureaucratic systems like FDA to be thoughtful in how they iterate their internal concepts and approaches. An open and transparent process will allow a continuing system of learning as new therapies and new unmet needs are addressed so that they are appropriately compensated by CMS and CMS is part of the societal solution and not a barrier to therapy development.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact Monica Davis by telephone at 303 547 3448 or by e-mail at monica.davis@cerebraltherapeutics.com if you have any questions regarding our comments.

Sincerely,

Daniel J. Abrams, MD

Cerebral Therapeutics, Inc.

12635 Montview Boulevard, Suite 137, Aurora, CO 80010 // 3510 Hopkins Place N, Building 4, Oakdale, MN 55128



Chronic Care Policy Alliance

State Advocates
Working Together
to Bridge the Gaps
in Chronic Care

April 13, 2023

Meena Seshamani, M.D., Ph.D.
Deputy Administrator and Director of the Center for Medicare
Centers for Medicare and Medicaid Services
U.S. Department of Health and Human Services

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Electronically Submitted via
IRAREbateandNegotiation@cms.hhs.gov

Dear Dr. Seshamani,

Thank you for the opportunity to provide comment on initial guidance implementing the Medicare Drug Price Negotiation Program of the Inflation Reduction Act.

The Chronic Care Policy Alliance (CCPA) is a network of state and regional advocacy organizations advancing public policy that improves the lives of those living with chronic conditions and diseases. Dedicated to achieving better access to quality, affordable health care, CCPA brings together advocates who share common goals and lends its experience in legislative action and public policy creation to support statewide and regional networking development.

1. Introduction – Guaranteeing A Patient-Centered Process

Ensuring that health programs and policies are patient-centered is paramount in producing the best outcomes for patients. Patients depend on access to care and treatments, and this is especially true for patients living with chronic diseases. According to the Centers for Disease Control and Prevention, 6 in 10 American adults live with a chronic disease, and 4 in 10 live with two or more.¹ For these patients, new therapies can have a life-changing impact – and importantly, for those patients still waiting on a “miracle” treatment for their condition, any policy that might delay that scientific achievement or create new barriers to accessing those treatments is a problem for patients.

While we understand that much of the Medicare Drug Price Negotiation Program’s initial guidance memorandum focuses on the interaction between the Centers for Medicare and Medicaid Services (CMS) and pharmaceutical manufacturers, the input of patients and the holistic impact on their care and availability of future treatments must be considered for this program to truly maintain a patient-centered orientation.

¹ <https://www.cdc.gov/chronicdisease/pdf/infographics/chronic-disease-in-america-H.pdf>

Recently, CCPA and 35 patient organizations sent a letter to CMS and Congress urging that the implementation of the Negotiation Program include patient voices in both the implementation and execution of the law – that letter is attached to these comments. We hope that CMS recognizes the broad support within the patient community for ensuring our voices are heard and that patients remain the focus of improving the health care system.

With that patient-centered orientation in mind, CCPA offers the following comments on the Negotiation Program’s initial guidance memo.

2. Patients Should Have a Role in Drug Selection

In Section 30 of the initial memorandum, CMS proposes to implement section 1192(a) of the Social Security Act by generating a list of the top 50 highest spend Negotiation-Eligible Drugs and then simply selecting the top 10 for negotiation.

However, we believe that the statute gives the Secretary flexibility in how to select the 10 drugs and that the statute does not require selecting the top drugs in descending order. Rather the statute directs the Secretary to “select from” the drugs with the “highest such rankings.”² CCPA believes that the Secretary should exercise this discretion to have a more thoughtful approach in the selection of drugs for negotiation.

CCPA is disappointed that CMS chose to issue Section 30 as final guidance, instead of as initial guidance open for comment as with the rest of the memorandum; patients must be afforded the opportunity to have their perspectives and views heard and incorporated into this process. We recommend that CMS use its authority to revise this section of the initial guidance memorandum to “open for comment.”

CCPA believes that the selection of drugs for negotiation should have public and patient input, and there should be a more nuanced and thoughtful process for selecting drugs for negotiation. Using a spending-only approach for selection ignores ongoing research for additional indications or new formulations for existing products that could have additional benefits such as greater adherence or reduced side effects. It also ignores the potential for unintended consequences of selecting a drug without considering other factors such as anticipated supply shortages. This rigid and inflexible approach has the potential to create unintended consequences by shackling the decision-making of CMS and limiting the ability of the agency to change course when problems arise.

Patients should have the ability to comment and have their input considered. Patients should be able to convey their views on what manufacturers are saying about ongoing research into new indications for drugs eligible for negotiation. For example, if a manufacturer is conducting ongoing research into a new indication for an existing product and the manufacturer indicates that negotiation may jeopardize that research, patients with that condition have an obvious interest in ensuring that continues.

² Social Security Act §1192(b)(1)(B) [42 USC §1320f-1(b)(1)(B)]

The Negotiation Program should be about what is best for patients – not what is simply best for the federal government’s financial considerations. At the end of the day, patients must be at the center of decision-making in Medicare.

3. During Negotiations, Patient Input Should Be Considered in a Broader Way

In Section 50.2 of the memorandum, CMS notes how patients and other stakeholders may provide input on alternative treatments and comparative effectiveness research of a drug selected for negotiation.

CCPA believes that CMS should solicit patient input beyond simply commentary on comparative effectiveness research and alternative treatments. CMS should hear direct patient impact statements, such as how a drug has made a meaningful difference in their life and well-being. Only considering sterile and anodyne research ignores the human factor in determining what is best for patients. While we value considering information in a data-driven, systematic way, other entities within the federal government charged with making scientific and policy-driven decisions understand the need to also evaluate patient impact. They routinely hear direct testimony from patients. These are not anecdotes replacing data – these are patients speaking truth to power. For example, advisory committees convened by the Food and Drug Administration routinely hear public comments as part of their meetings. This testimony supplements, not supplants, the data-driven and scientific considerations made by these advisory committees.

Only by factoring in patient narratives about the impact of a treatment can CMS fully grasp the value a product provides to treat chronic conditions and diseases. This is an important pillar of our nation’s drug development ecosystem – patients want products to be rewarded for their value, because this underpins the development of new treatments. Patients want the robust incentives for drug development that have brought thousands of new products to market over the last 30 years to continue.

4. Patients Should Be Protected Through Part D Plan Requirements

In Section 110 of the memorandum, CMS details requirements on Part D plans for negotiated products. CCPA believes that CMS must create requirements on Part D plans related to both the negotiated product and non-negotiated products with the same indication.

A. Negotiated Products

In Section 110 of the memo, CMS will require Part D plans to cover negotiated products. This is a good first step. CMS should also require that all plans cover these products 1) on the tier of their formulary most favorable to patients; 2) without prior authorization; and 3) without other utilization management requirements, or with requirements that match other products for the same indication.

A risk with the Medicare Drug Price Negotiation Program is that Part D plans will favor negotiated products over non-negotiated products. Patients for whom a non-negotiated product is the best option for them and potentially the only option, as determined by their physician, should not be

inadvertently disadvantaged by plans clustering coverage around a negotiated product. Not all patients have the ability to switch products, even among products for the same indication. In some cases, transitioning between products can have detrimental effects. Ensuring patients are able to continue using their existing products without facing higher cost-sharing or new hurdles is important.

B. Non-Negotiated Products for the Same Indication

For non-negotiated products for the same indication as a negotiated product, CMS should utilize its authority to ensure patient access is prioritized. While there are numerous forms this could take, one step we recommend is that CMS prioritize ensuring there is a robust and meaningful appeals process for beneficiaries who need an alternative product other than the negotiated product.

Ensuring parity between negotiated and non-negotiated products will prevent disruptions or new expenses for patients. This is especially important for patients with chronic conditions that are well-managed with a specific treatment and fear being pushed (by cost or coverage policy) into a different treatment.

5. Conclusion

Again, thank you for the opportunity to provide comment on the initial guidance memorandum. CCPA hopes that opportunities to provide comment will continue throughout the implementation and negotiation process. CCPA urges CMS to consider other avenues for patient input, such as through listening sessions, roundtables, or other forums. We view patient-advocacy as an ongoing dialogue, and we hope to continue having opportunities to represent the views of patients with chronic diseases.

For patients, health care policies should not be made “about us, without us” – patients must have a seat at the table and have their voices heard.

Sincerely,



Liz Helms
Founder/Director
Chronic Care Policy Alliance
1001 K ST. 6th Floor
Sacramento, CA 95814
www.chroniccarealliance.org

Attachment

In a letter to Congress and the Centers for Medicare & Medicaid Services (CMS), the Chronic Care Policy Alliance (CCPA) was joined by 35 organizations urging Congress and the Administration to ensure that patient advocates have a seat at the table throughout the implementation of the Inflation Reduction Act's health policies. CCPA and its partners want to protect patient interests and avoid any unintended consequences by asking for patient input in the planning phase before implementation. Read the full letter:

Dear Congress/CMS:

As patient representatives, we advocate on behalf of patient interests and interpret how certain policies will positively or negatively affect them. Patients know firsthand the benefits of a strong health care system that provides access to new and groundbreaking treatments. In recent years, we have seen great strides in the treatment of ALS, cancer and Alzheimer's disease that have increased lifespan, slowed the ravage of disease and improved the quality of lives.

Last year, Congress passed significant policies within the Inflation Reduction Act (IRA) focused specifically on patient costs. We were especially pleased by the improvements to Medicare Part D that included adding an out-of-pocket cap, establishing a \$35 limit on monthly insulin costs, and eliminating cost sharing for vaccines. These policies will provide immediate relief to patients. Thank you.

However, other policies around prescription drug prices faced significant debate during the legislative process. Policymakers must keep in mind the unknown long-term impacts on the development of new treatments – especially those for complex and rare diseases – and patients' ability to access those new therapies.

Now it is time for the real work as the Administration begins the lengthy process of implementing IRA's policies. We urge Congress to continue oversight throughout the implementation process and insist that patient voices are heard.

The Medicare Drug Price Negotiation Program contained in the law seeks to establish negotiated rates, or the Maximum Fair Price (MFP), for medications. While focused on reducing drug costs, the unintended negative consequences for drug coverage, formulary priority, access and further research and development could harm patients. For example, as new prices are determined, payors may favor products on their formularies that have a negotiated price. This could ultimately make other medications more difficult to access as payors encourage use of these negotiated price medications and discourage others. Payors already utilize cost saving measures that negatively impact patients such as restrictive formularies, step therapy and strict prior authorizations. Patients need access to the correct treatments, or they will suffer. The addition of products with artificially lowered prices is likely to create yet another restrictive process for patients.

We urge Congress to ensure that regulators at CMS create specific opportunities for patient advocates to participate in the regulatory process.

Our specific recommendations include:

- **Host regional roundtables to solicit feedback from patients.** We strongly recommend that CMS create a structure similar to that used to implement the Affordable Care Act (ACA) and utilize the CMS regional staff to hold patient-centered roundtable discussions throughout the country to ensure that patients have the opportunity to share their experiences and insights directly with CMS, regardless of their physical location. Providing regional opportunities is

particularly important in the patient community where resources may make participation at the federal level more of a challenge than in their state and local communities.

- **Release draft guidance, solicit written comments.** We are pleased that CMS has announced that it will issue draft guidance that seeks public input on key provisions of the MFP program. We hope that the draft guidance includes and seeks feedback on the process, including the methodology CMS uses to determine the MFP. Soliciting written comments from the public is critical.
- **Develop patient-centered criteria.** CMS should also develop, with significant input from patients, patient-centered criteria that must be adhered to as CMS implements the drug pricing provisions. This will ensure patient perspectives are heard and patient needs are prioritized. The ACA required that the Center for Medicare and Medicaid Innovation develop similar criteria.
- **Meaningfully engage patients in determining the MFP for each drug.** Patient advocates can offer both substantial and critical perspectives as CMS considers what a price should be for a specific drug. CMS should create a process through which it will consistently and meaningfully engage with patients determining each drug's price, and ensure they have a say in the outcome.
- **Study the impact of the drug pricing provisions on patients.** CMS should study the impact that negotiation has on patients prior to negotiation, focusing on issues related to access to current and future therapies. For example, CMS should study the impact of the drug pricing provisions on Medicare Part D coverage, including formulary placement and utilization management.

Should you have any questions or comments, please contact Liz Helms, Founding Director, CCPA at lizh@chroniccarealliance.org. Thank you for your time and attention to these critical issues.

Sincerely,

Chronic Care Policy Alliance (CCPA)

Alliance for Aging Research; ALLvanza; American Behcet's Disease Association (ABDA); Applied Pharmacy Solutions; Autoimmune Association; Axis Advocacy; Black, Gifted & Whole Foundation; Cancer Support Community; Chronic Disease Coalition; Coalition of Wisconsin Aging and Health Groups; Colorado Gerontological Society; GO2 for Lung Cancer; Healthy Men Inc.; Hereditary Neuropathy Foundation; HIV + Hepatitis Policy Institute; ICAN, International Cancer Advocacy Network; International Foundation for AiArthritis; Lazarex Cancer Foundation; Let's Talk About Change; Looms For Lupus; Men's Health Network; MLD Foundation; National Association of Nutrition and Aging Services Programs (NANASP); National Hispanic Medical Association; National Patient Advocate Foundation; National Puerto Rican Chamber of Commerce; Neuropathy Action Foundation (NAF); Nevada Chronic Care Collaborative; Partnership for Innovation and Empowerment; Partnership to Fight Chronic Disease; Patients Rising Now; RetireSafe; Southern Christian Leadership Global Policy Initiative (SCL-GPI); Support For People With Oral And Head And Neck Cancer, Inc. (SPOHNC); The National Puerto Rican Chamber of Commerce



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April 14, 2023

VIA ELECTRONIC SUBMISSION TO IRAREbateandNegotiation@cms.hhs.gov

Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: Medicare Drug Price Negotiation Program Guidance
P.O. Box 8013
Baltimore, MD 21244-8013

**Re: Medicare Drug Price Negotiation Program Guidance: Initial Memorandum,
Implementation of Section 1191-1198 off the Social Security Act for Initial Price
Applicability Year 2026, and Solicitation of Comments**

To Whom It May Concern:

The Cigna Group welcomes the opportunity to respond to the Medicare Drug Price Negotiation Guidance Initial Memorandum ("Initial Guidance"). Cigna appreciates the Centers for Medicare and Medicaid Services' (CMS) efforts to improve prescription drug affordability for Medicare beneficiaries. We provide detailed feedback on key areas of the Initial Guidance below.

The Cigna Group is a global health services organization committed to improving health and vitality. Our Cigna Healthcare and Evernorth Health Services divisions are major providers of medical, pharmacy, dental, and related products and services, with over 190 million customer relationships in the more than 30 countries and jurisdictions in which we operate. Within the United States, Cigna provides medical coverage to approximately 14.9 million Americans in the commercial group health plan market, predominantly in the self-insured segment. For 2023, we will be providing coverage in the individual Affordable Care Act insurance segment in sixteen states, both on- and off-Exchange, to more than 770,000 people. Additionally, we serve approximately 4.4 million people through our Medicare Advantage (MA), Medicare Prescription Drug Program and Medicare Supplemental products. In all of the segments we serve, Cigna is focused on working to deliver health care that is affordable, predictable, and simple – so people can live healthier, more vibrant lives.

Overall, Cigna thanks CMS for its approach to providing both this Initial Guidance with solicitation for comments, as well as the timeline CMS has publicized for its Inflation Reduction Act (IRA) implementation efforts. Cigna supports the transparent nature of CMS's effort to provide a roadmap for its IRA implementation work. By sharing the anticipated steps CMS plans to take, stakeholders will be better able to provide meaningful comments that will ultimately enable CMS to improve the Medicare Drug Price Negotiation program. Cigna looks forward to working collaboratively with CMS as IRA implementation proceeds.

We have three main comments on the Initial Guidance that we would like to raise. First, Cigna encourages CMS to confirm that Part D plan sponsors continue to possess the ability to use utilization management and formulary management tools as appropriate, to promote clinically sound, cost-effective medication therapy, and positive therapeutic outcomes. Second, we are concerned that CMS's approach to identifying potential qualifying single source drugs (QSSDs) is overly broad and may result in unintended consequences for patient access. CMS's approach would aggregate drug products with different modes of administration into a single potential QSSD and we are concerned regarding the considerable cost variation among drug products that may result. Third, Cigna is supportive of the development and marketing of biosimilars to generate competition within the market and is concerned that the requirements for an Initial Delay Request may discourage biosimilar development.

Consistent with these concerns, Cigna offers the following key recommendations:

- CMS should confirm that Part D plan sponsors are permitted to use utilization management tools and formulary management tools as appropriate, to promote clinically sound, cost-effective medication therapy, and positive therapeutic outcomes associated with selected drugs.
- Drugs with the same active ingredient, but different modes of administration should not be included in the definition of a potential QSSD.
- The requirements that must be met for an Initial Delay Request for biologics should be more objective and less subjective in nature; consideration should be given to how stringent those requirements are and whether they could increase barriers to entry for biosimilars.

Cigna's detailed recommendations are provided below in their corresponding Initial Guidance sections.

Section 30 – Identification of Selected Drugs for Initial Price Applicability year 2026

Section 30.1. Identification of Qualifying Single Source Part D Drugs for Initial Price Applicability Year 2026

Under the Initial Guidance, CMS intends to include all dosage forms and strengths of the drug with the same active moiety and the same holder of a New Drug Application (NDA) or Biologics License Application (BLA) as a single potential QSSD.

Cigna Comments: While Cigna recognizes that Section 30 is final without comment solicitation, we would like to take this opportunity to address the potential unintended consequences of the approach to identifying QSSDs. We understand that CMS is attempting to prevent gamesmanship around patents and follow-on products, but Cigna believes that this definition is overly broad. By using this broad approach, CMS may be increasing the risk of unintended consequences associated with its negotiated pricing, simply because more drug products with varied characteristics will be swept into a single potential QSSD. This broad approach may present issues for patient access to the extent that prices may not be viable for some manufacturers, causing some products to be discontinued. We urge CMS to consider this issue and its effects for patient care. In particular, Cigna is concerned regarding CMS's approach to products with the same active ingredient, but different modes of administration. To this end, we offer the following recommendations.

Drugs with the same active ingredient, but different modes of administration should not be included in the definition of potential QSSD. Price applicability year 2026 is limited to Part D drugs, which are typically self-administered. However, there are instances in which one product has several different modes of administration, such as oral, subcutaneous, or infused. These different modes of administration could lead to CMS to have to identify separate Part D and Part B products as a single product, despite the first year being limited to Part D drugs.

Additionally, Cigna believes there is substantial cost variation associated with the mode of administration and nothing in statute requires CMS to aggregate a single drug across modes of administration. We recommend that CMS treat each mode of administration as its own QSSD to ensure that the cost associated with each mode is accurately reflected in the MFP.

Section 30.3.1. Delay in the Selection and Negotiation of Certain Biologics with High Likelihood of Biosimilar Market Entry

In accordance with statute, CMS outlines the seven requirements that must be met in order for the agency to grant an Initial Delay Request, including that: the request must be made by the biosimilar manufacturer; the biosimilar manufacturer cannot be the same as the reference manufacturer; a request cannot be made if a year has elapsed since the biosimilar was licensed, but no marketing has commenced; and CMS must determine that there is a high likelihood that the biosimilar will be licensed and marketed before the date that is two years after the selected drug publication date.

The Initial Guidance also stipulates that in order for an Initial Delay Request to meet the high likelihood threshold, CMS will determine if the following are met:

- An application for licensure under section 351(k) of the Public Health Service (PHS) for the biosimilar has been accepted or approved by the Food and Drug Administration (FDA); and
- There must be clear and convincing evidence that the biosimilar will be marketed before September 1, 2025, based on information submitted to CMS.

Such information includes demonstrating that the patents related to the reference product are unlikely to prevent the biosimilar from being marketed and that the biosimilar manufacturer will be operationally ready to market the biosimilar. CMS notes that these were selected as they are the two primary contributing factors to delay in marketing biosimilars approved in the United States. As part of this process, CMS must also evaluate if there is ongoing litigation related to the licensure and marketing of the biosimilar.

Cigna Comments: Cigna believes that CMS's approach to identifying forthcoming biosimilar competition is overly stringent and subjective in nature. While CMS identifies numerous factors in which it will assess the high likelihood requirements against, it does not provide a clearly defined threshold that biosimilar drugs must meet to demonstrate its high likelihood. Cigna recommends that the benchmark CMS utilizes to trigger the delay or removal from negotiations be more transparent and objective.

Additionally, as written, these requirements create reporting standards that are more burdensome than what is required of selected drugs and could create an additional barrier for biosimilar drug development. If CMS wants to support biosimilar development and therefore greater competition in the pharmaceutical market, the agency should ease the threshold burden for biosimilar manufacturers to obtain an Initial Delay. For example, a biosimilar manufacturer's submission of a marketing plan should be weighed heavily as a factor toward the high likelihood threshold.

Cigna is also concerned with CMS's proposed use of litigation as a qualifying factor in the high likelihood threshold. The requirement to evaluate litigation may result in reference manufacturers engaging in additional litigation. It is far too easy to file a complaint that would yield substantial benefit for manufacturers of reference products.

Finally, Cigna would like to express support for requiring that the biosimilar manufacturer differ from the reference manufacturer for the initial delay request to be granted. Cigna also supports not granting an initial delay request if more than one year has elapsed since the licensure of the biosimilar and marketing of the biosimilar has not commenced. We believe this aligns with the intent of the law to delay or remove biologics that will be subject to meaningful competition at the time of price applicability.

Section 40 – Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026

CMS intends to designate the manufacturer that holds the NDA(s)/BLA(s) for the selected drug to be the "Primary Manufacturer." The "Secondary Manufacturer" would include any manufacturers of any authorized generics and any repacker or relabeler of the selected drug that meet these criteria. CMS intends to enter into a Medicare Drug Price Negotiation Program Agreement with the Primary Manufacturer ("Agreement") and not any Secondary Manufacturer. CMS intends to include in the Agreement with the Primary Manufacturer several requirements pertaining to Secondary Manufacturers of the selected drug. Further, CMS intends to require that Primary Manufacturers ensure that any Secondary Manufacturer of a selected drug make the MFP available to Part D plan sponsors and dispensers.

Cigna Comments: Cigna supports holding Primary Manufacturers responsible for requirements pertaining to Secondary Manufacturers. We agree that this approach aligns with the statute's requirement for CMS to determine an MFP with "the manufacturer" of a selected drug. Further, centralizing responsibility for compliance with Primary Manufacturers will allow CMS to operationalize the requirements of the Medicare Drug Price Negotiation Program most efficiently.

40.2 Submission of Data to Inform Negotiation

CMS intends to require the Primary Manufacturer of a selected drug to submit data to inform the negotiation process for initial price applicability year 2026 by October 2, 2023. Data elements will include information on the non-Federal average manufacturer price and any information that CMS requires to carry out negotiation, including research and development costs, current unit costs of production and distribution, prior Federal financial support, data on pending and approved patent applications, and market data and revenue and sales volume data.

CMS intends to treat information on non-Federal average manufacturer price and certain data elements as proprietary information, protected from disclosure under Exemption 4 of the Freedom of Information Act and only available for use by CMS and the Comptroller General of the United States. CMS intends to make high-level comments about the data submitted to CMS, without sharing any proprietary information report to CMS.

Cigna Comments: Cigna thanks CMS for seeking input about the proper balance between the public's interest in transparency and the protection of business information within the context of the Negotiation Program. We agree that non-public data should remain proprietary. However, the provision of "high-level comments" in conjunction with the publication of MFPs is insufficient. Understanding the factors and rationale that serve as the basis for MFP is fundamental for plans and PBMs to negotiate lower prices on behalf of beneficiaries. Cigna urges CMS to disclose, at a minimum, factors that have a material impact on MFP, such as comparative effectiveness analysis.

40.4 Providing Access to the MFP

CMS intends to require that Primary Manufacturers provide access to the MFP to Part D plan sponsors and dispensers (e.g., pharmacies) in one of two ways: (1) ensuring the price paid by the dispenser when acquiring the drug is no greater than MFP; or (2) providing retrospective reimbursement for the difference between the dispensing entity's acquisition cost and the MFP. CMS intends to allow access to MFP by Part D plan sponsors and dispensers either at the point of sale or through the provision of retrospective reimbursement for the difference. CMS intends to require that Primary Manufacturers ensure that dispensers as well as intermediary entities, such as wholesalers, are reimbursed timely for the difference between their acquisition cost and the MFP within 14 days. As noted above, CMS intends to require that Primary Manufacturers ensure that any Secondary Manufacturer of a selected drug make the MFP available to Part D plan sponsors and dispensers.

Cigna Comments: Cigna supports the creation of a process for Primary Manufacturers to provide access to the MFP. However, we caution against providing manufacturers with excessive latitude in how to provide access to the MFP. We appreciate that the mechanism under which the Negotiation Program will operate mirrors the Coverage Gap Discount Program (CGDP). This approach ensures eligible Medicare beneficiaries will have access to the MFP at the point of sale and see cost sharing relief.

Consistent with this approach, Cigna recommends that CMS explicitly delineate in final guidance the role of pharmacy benefit managers (PBMs) in facilitating access to the MFP at the point of sale, making PBMs the intermediary in this process. PBMs have the data needed to serve as the appropriate intermediary, protecting beneficiaries from extremes and holding pharmacies harmless. Further, operating MDP and MFP in the same system is the best solution because MFP-priced drugs are excluded from MDP. This has the added benefit of reducing unnecessary manufacturer disputes, if the same TPA is processing both kinds of discounts in the same way, and in the same time frame.

40.4.1 Nonduplication with 340B Ceiling Price

CMS intends to require Primary Manufacturers to provide a 340B covered entity with access to the MFP for a selected drug furnished, administered, or dispensed to an MFP-eligible individual if the MFP is below the 340B ceiling price for the select drug. The Primary Manufacturer would not be required to provide a 340B covered entity with access to the MFP if the 340B ceiling price is lower than the MFP.

Cigna Comments: Cigna understands CMS's concern regarding potential duplication with the 340B Drug Pricing Program. We recommend that CMS consider publishing a database, similar to the [340B Office of Pharmacy Affairs Information System](#), that makes MFPs for selected drugs publicly available or consider working with Health Resources and Services Administration (HRSA) to add MFPs to this existing system.

Section 110 – Part D Formulary Inclusion of Selected Drugs

CMS proposes to require Part D plans to include each covered Part D drug that is a selected drug on formularies during Contract Year 2026 and all subsequent years for which the MFP of the selected drug is in effect during the price applicability period.

Cigna Comments: There is no requirement in the IRA regarding how selected drugs are to be included in Part D formularies. Consistent with section 1860D-4(b)(3)(I)(ii) of the Social Security Act, we urge CMS to confirm Part D plans' formulary flexibilities for selected drugs. Part D plans design and manage formularies based on input from Pharmacy and Therapeutics (P&T) committees and scientific evidence to ensure beneficiary access to safe and clinically appropriate access to drug therapies. We also encourage CMS to clarify when the formulary inclusion requirement would not apply, such as when a generic or biosimilar comes to market for a selected drug that is on the formulary.

Conclusion

Thank you for your consideration of these comments as we work together to improve prescription drug affordability for Medicare beneficiaries. Cigna would welcome the opportunity to discuss these issues with you in more detail at your convenience.

Respectfully,



Kristin Julason Damato



Thomas A. Schatz, *President*
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Washington, D.C. 20036
ccagw.org

April 14, 2023

Administrator Chiquita Brooks-LaSure
Centers for Medicare & Medicaid Services
Department of Health and Human Services
500 Security Boulevard
Baltimore, MD 21244

Re: “Medicare Drug Price Negotiation Program Guidance.”

Dear Administrator Brooks-LaSure,

On behalf of the more than one million members and supporters of Citizens Against Government Waste (CAGW), I respectfully submit these comments to the Centers for Medicare & Medicaid Services (CMS) in response to its March 23, 2023, solicitation for comments regarding its “initial guidance for implementation of the Negotiation Program for initial price applicability year 2026.”

The CMS guidance is being provided following the enactment of [Inflation Reduction Act](#) (IRA), which was signed into law on August 16, 2022. As CAGW [wrote](#), the Medicare drug negotiation [provisions](#) create [price controls](#) that will dramatically undermine drug research and development and [leave](#) “an [invisible graveyard](#) of patients.” Government price-setting will neither improve access to care nor lower patient costs. And giving the secretary of Health and Human Services (HHS) the authority to set prices at the maximum fair price (MFP) is not a negotiation, it is a mandate.

In their April 13, 2023, [letter](#) to you and HHS Secretary Xavier Becerra, Senate Finance Committee Ranking Member Mike Crapo (R-Idaho), House Energy and Commerce Chair Cathy McMorris-Rodgers (R-Wash.), and House Ways and Means Committee Chairman Jason Smith (R-Ark.) wrote that the initial guidance should be reconsidered because it would impede innovation, weaken intellectual property (IP) protection, and hurt research into new uses for a drug. They also expressed the concerns that the guidance would be a “backdoor mechanism” to implement march-in rights in violation of the Bayh-Dole Act, which was enacted at a time when few inventions or discoveries funded by government grants were being commercialized. The act allowed patents owned by government-funded research entities to be transferred to private companies, which would spend money at their own risk to commercialize the discoveries. “March-in rights” were only permitted if the private sector collaborator failed to commercialize the invention. Undermining Bayh-Dole would further erode IP protection. We agree with these concerns about the initial guidance.

With respect to the time allowed to respond to the initial guidance, most federal agencies provide a 60-day comment period with a 30-day period for reply comments, which has not been

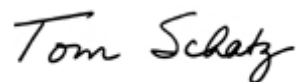
afforded in this proceeding. The impact of the guidance on research and development, intellectual property, drug pricing, government control of the pharmaceutical industry, and the live and death of current and future patients certainly requires more time than CMS has permitted for comments.

The proposed guidance threatens future innovation by setting rules and regulations that further devalue existing patents and IP rights for specific drugs. Research and development after Food and Drug Administration (FDA) approval is necessary to develop future cures. The proposed CMS guidance will disincentivize research and development post-approval and drug manufacturers could potentially be penalized with a lower MFP.

Another objectionable aspect of the proposed guidance is the “gag” rule that would require a drug manufacturer to hide and destroy information related to each individual decision on drug pricing. The proposed restrictions would be contrary to Freedom of Information Act (FOIA) and document retention standards. Hiding the underlying basis for a decision on drug pricing subverts accountability and transparency. It could also be considered as a prior governmental restraint on speech in violation of the First Amendment.

If CMS proceeds with implementation of the proposed guidance, there will be a significant negative impact on drug manufacturers and their ability to develop safe and effective drugs, as well as devastating consequences for patients now and well into the future. CAGW urges CMS to implement a longer comment period and eliminate provisions in the proposed guidance that would have negative implications on research and development, transparency in government, and freedom of speech.

Sincerely,

A handwritten signature in black ink that reads "Tom Schatz". The signature is written in a cursive, slightly slanted style.



VIA ELECTRONIC DELIVERY

April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244-1850

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026

Dear Administrator Brooks-LaSure:

CLL Society appreciates the opportunity to submit its comments on the Centers for Medicare & Medicaid Services' (CMS') Initial Guidance on implementation of the Drug Price Negotiation Program created under the Inflation Reduction Act of 2022 (IRA).

CLL Society is dedicated to addressing the unmet needs of the chronic lymphocytic leukemia and small lymphocytic lymphoma (CLL/SLL) community through patient education, advocacy, support, and research. Our patients live with a chronic, rare cancer of the immune system. We are the largest nonprofit focused exclusively on the unmet needs of patients living with CLL and SLL.

We strive to fulfill our primary mission of ensuring that patients have access to safe and effective treatment options by informing patients and caregivers about the rapidly changing therapeutic landscape and the importance of clinical trials, supporting, and building patient networks, engaging in research, and educating providers and patients. As an organization, we also recognize that the healthcare landscape extends beyond science, clinical care, and patient support. Legislative, regulatory, and policy initiatives have the potential to exert a considerable and increasing force on equitable access to existing treatments and the development of new therapeutic options.

CLL Society expects that the IRA provisions capping Part D out-of-pocket costs will bring substantial relief to our patient community. Just as importantly, CMS' implementation of a "smoothing" mechanism will allow patients to spread their out-of-pocket costs over the year and avoid the all-too-common scenario of having to base treatment decisions on their financial concerns rather than their medical needs.

While the drug price negotiation program may have a marginal impact on healthcare costs for patients with relatively common conditions, as well as CLL and SLL patients who are not currently receiving active treatment, it will likely have no impact on out-of-pocket costs for patients requiring



active therapy. There is little doubt that the decisions CMS makes now on the price negotiation program will become part of the complex calculations researchers, investors, and drug manufacturers make when determining whether to pursue a particular drug candidate for a specific indication. We fear that without a proactive intent to preserve the fragile cost/benefit balance in small population diseases, CMS will inadvertently tip the scales away from innovation in CLL and SLL as well as other related blood cancers.

Our comments provide a brief background on the disease and focus on the potential impact that the policies and processes within CMS' Initial Guidance might have on our patient community. We urge CMS to exercise its implementation discretion to ensure that our health system continues to welcome the rapid scientific advances in our understanding of disease mechanisms and targeted treatment approaches that have driven hope for blood cancer patients and their families.

Background

CLL is a chronic blood cancer of a type of white blood cell called the B-lymphocyte. In CLL there is a progressive accumulation of too many mature B-lymphocytes. CLL is the most common leukemia in adults in the United States, with around 21,000 cases diagnosed annually. Besides being a type of leukemia, it is also classified as a type of non-Hodgkin's Lymphoma (NHL). So CLL is both leukemia and lymphoma at the same time. SLL is simply a different manifestation of the same disease and is best understood as a different stage of CLL where there are not a significant number of cancer cells yet located in the bloodstream. When the cancer is only found in the lymph nodes it is called SLL. When the cancer is found in the bloodstream and possibly elsewhere, including lymph nodes, it's called CLL.

CLL/SLL is extremely heterogeneous, meaning each person's disease course and progression can be extremely variable. Some experience rapid deterioration due to having an aggressive form of the disease and survive for as little as two years, while some who have a less aggressive form of the disease will never need treatment and can expect to have a normal life expectancy.

Targeted therapies such as BTK inhibitors and the BCL2 inhibitor known as venetoclax offer substantial efficacy against CLL/SLL and have transformed care for our patient community. Patients now have more treatment options compared to just years ago when the standard of care was chemoimmunotherapy. They can take continuous daily oral therapy with a BTK inhibitor, with or without a monoclonal antibody, until their disease progresses. Alternatively, patients can choose a short-term time-limited treatment approach that combines venetoclax and a monoclonal antibody. The latter approach enables dose discontinuation until active monitoring reveals that another treatment is needed.

Although most CLL/SLL patients can expect a response to initial therapy, nearly all current treatment options are palliative and not curative. Most patients will experience one or more



relapses during the course of their disease, and many are forced to either change treatments, take a “drug holiday,” or adjust dosing due to drug intolerance. For patients with relapsed or refractory disease (or treatment intolerance), treatment decisions are highly individualized based on prior therapies, prior response, the reason for discontinuation of previous therapy, comorbidities, biomarker characteristics, patient preference, and therapeutic goals. Patients can experience serial relapses, and many will be treated with all available agents at some point during their disease course.

The unfortunate reality is that despite significant progress in treating CLL/SLL, it remains an incurable cancer. Patients progressing after both BTK and BCL2 inhibitors face a poor prognosis with few treatment options other than PI3K inhibitors. Unfortunately, the use of PI3K inhibitors for hematologic malignancies has recently come under scrutiny due to safety and efficacy concerns. Manufacturers have voluntarily withdrawn indications for idelalisib in both follicular lymphoma (FL) and SLL, and duvelisib in FL. Additionally, umbralisib was completely withdrawn from the market. The FDA’s recent ODAC meeting recommended the withdrawal of duvelisib. If this comes to pass, there will be no available PI3K inhibitor approved as a single agent in CLL, and none at all in SLL.

The experience with PI3K inhibitors in CLL/SLL illustrates the inherent difficulties surrounding studying this disease and the heightened risk manufacturers take on when pursuing new therapeutic candidates. Delays associated with the wait for overall survival data have already dampened research efforts and slowed patient access to potentially life-saving therapies. We have advocated for crossover in clinical trials to save lives, but the strategy inherently compromises the “purity” of survival data. Since CLL/SLL is not an ideal disease state from a research perspective, “new” treatments are often first approved for other cancers and then later approved for CLL/SLL under FDA’s accelerated approval mechanism. Research and development efforts in CLL/SLL could be significantly deterred due to the combination of increased payer hesitance to fully cover and pay for accelerated approval therapies, and the likelihood that a CLL/SLL indication would render an existing drug ineligible for the IRA orphan exclusion to price negotiation, slowing new drug development in CLL/SLL and other rare cancers. We are concerned that this evolving landscape, viewed holistically, poses dire consequences for CLL/SLL patients as they exhaust available treatment options.

CMS should extend the time for stakeholder feedback on the Initial Guidance.

CLL Society has reviewed the complex set of policies within the Initial Guidance with an eye toward identifying concerns within our patient and provider communities and making recommendations to address those concerns. We had hoped that CMS would fulfill its commitment to prioritize transparency and robust engagement in implementing the price negotiation program. Unfortunately, CMS has issued “final” guidance to implement policy decisions we did not anticipate in light of the statutory language, that importantly warrant public input and will likely drive the success or failure of the program. To the extent that CMS reached out to the patient advocacy



community in advance of issuing the Initial Guidance, we were unaware of the approach CMS was considering, much less the opportunity to shape alternative approaches.

We are also concerned that the Agency exposes itself to legal challenges that will inject considerable uncertainty among manufacturers, investors, and even private payers. Uncertainty is a highly disruptive force that can stall or deter access to the resources that fuel innovation. We urge CMS to consider stakeholder feedback received through the 30-day comment process and extend the time for additional comments on the entirety of the Initial Guidance. Going forward, we also respectfully request that CMS develop a review process that allows for a consistent and open dialogue with the patient community. For the countless patients hoping for new treatments and equitable access to existing options, the stakes are too high for CMS to prioritize expedience over inclusion and consideration.

Orphan Drug Exclusion

CLL Society appreciates CMS' interest in stakeholder ideas that might facilitate orphan drug development. We also generally support the Agency's decision to extend the orphan drug exclusion to drugs with a single designation (as opposed to a single indication). The small and emerging biotechnology companies responsible for over 80% of orphan product development are particularly vulnerable to landscape changes that can impact the recoupment of research and development costs.

The risk/benefit analysis is particularly complex within the context of CLL/SLL treatments. As noted above, BTK inhibitors offer considerable improvements in care for our patients but can result in drug intolerance requiring discontinuation. Zanubrutinib is a BTK inhibitor with an orphan designation and approval in the treatment of mantle cell lymphoma (2019) that has demonstrated fewer cases of atrial fibrillation than ibrutinib and no cardiac-related deaths. CLL/SLL patients taking zanubrutinib also have a higher response rate and a longer time to disease progression. The January 19, 2023, announcement that FDA had approved zanubrutinib for both CLL and SLL was particularly significant in that it worked well in patients with difficult-to-treat cancers (i.e., those with a mutated gene called TP53, or a chromosomal alteration known as a 17p deletion). We believe it is unlikely that the manufacturer would have invested in the studies required for this set of approvals if its label expansion would have rendered the drug ineligible for the orphan drug exclusion.

The reduced side effect profile for zanubrutinib will enable patients to remain on treatment longer, but once their disease progresses, they cannot simply switch to one of the other irreversibly binding BTK inhibitors approved for CLL/SLL and expect a response. This is because once a drug within that same drug class has failed the patient, all drugs within that same class will likely fail. The January 27, 2023, accelerated approval of reversibly binding BTK inhibitor pirtobrutinib for the treatment of mantle cell lymphoma was a significant advance in lymphoma treatment, as it is



indicated for relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, **including a BTK inhibitor**. This treatment has already demonstrated the potential to address a significant unmet need in CLL/SLL patients who have been failed by an irreversibly binding BTK inhibitor. We are pleased that Eli Lilly is moving forward with their clinical trials in CLL, and our patient communities are hopeful that these studies will result in an FDA-approved treatment for patients who have exhausted their existing options. As the drug price negotiation program becomes a tangible reality for manufacturers, however, there is a very real danger that it will drive decisions on the drug candidates and/or indications manufacturers and investors are willing to pursue.

The sets of incentives encouraging the development of treatments for small-population diseases have generally worked well to expand treatment options and improve survival for patients with CLL/SLL and other blood cancers. The IRA's narrow exclusion for orphan drugs, however, creates a landscape in which multiple designations for a promising therapy will negate eligibility for the exclusion, thereby substantially complicating analyses on the potential for favorable return on investment. Manufacturers may face pressures to focus on an orphan indication with the largest patient population rather than the disease state that is most suitable for clinical trials. This could impact the time it takes to move a product from bench to market, increase costs associated with securing a first approval, and deter studies in Waldenström's Macroglobulinemia and other blood cancers with extremely small patient populations.

We are similarly concerned that manufacturers will face considerable tension between their legal and fiduciary obligations to shareholders and their perceived moral obligation to cancer patients. Any decision to invest in research toward an expanded label that could ultimately disqualify the drug from the orphan drug exclusion would appear to be unsupportable if the follow-on indication population is small. Manufacturers may also face difficulties securing approval from their directors, shareholders, and investors to continue confirmatory studies for accelerated approval indications with small addressable populations if withdrawing those indications would make a drug eligible for the orphan drug exclusion. We do not believe Congress or the Administration sought to limit research and development in orphan diseases generally or in rare cancers. Manufacturers secured orphan designations well before the IRA was enacted and could not have considered that a relatively narrow designation would later drive consequences to research and development in other indications.

We believe researchers, investors, and manufacturers should be rewarded, not penalized, for investing in research and development to secure FDA approval for new indications (rather than relying on off-label use). It would be a tremendous tragedy if Congress' efforts to improve healthcare affordability created an environment in which future treatments like Pirtobrutinib would never be indicated for CLL/SLL (or mantle cell lymphoma) despite their potential to transform patient care. These concerns are compounded by the fact that the same considerations exist for other treatments with orphan designations outside CLL/SLL. Zanubrutinib, for example,



was first approved in 2019 for mantle cell lymphoma. Its MCL approvals, as well as the label expansion in relapsed or refractory marginal zone lymphoma (MZL), were granted through the accelerated approval mechanism and remain contingent upon the completion of confirmatory studies. Zanubrutinib's orphan designation is for mantle cell lymphoma, and each additional indication is outside that narrow designation, including the label expansions for CLL/SLL and WM that were secured through FDA's traditional approval mechanism. CLL Society expects that the IRA will make approval histories like that of Zanubrutinib a thing of the past, despite the significant benefit conferred to blood cancer patients from manufacturer-sponsored studies in multiple indications.

CLL Society asks that CMS support and pursue Congressional action to remove the single orphan designation/indication requirement for orphan drug exclusion eligibility. The statutory language as it stands leaves manufacturers with a no-win proposition and jeopardizes patient access to promising therapies without any benefit to the Medicare program or society as a whole. We also urge CMS to implement a stop-gap measure through its demonstration authority that would maintain the status quo with regard to payment mechanisms (e.g., ASP-based), and apply to orphan drugs that do not have annual utilization in any one indication that exceeds 200,000 patients.

In addition, we urge CMS to enable manufacturers to submit evidence demonstrating eligibility for the orphan drug exclusion.

Definition of Qualifying Single Source Drug

CLL Society urges CMS to reconsider its decision to identify a qualifying single source drug, and its dosage forms and strengths, by referring to common active moiety (drugs) or common active ingredient (biologics). The approach that CMS has chosen is not mandated by the statutory language. In fact, the IRA appears to require that products be treated as the same qualifying single-source drug only when they share an NDA or BLA. The determination of negotiation eligibility for products approved through an NDA [or BLA] is based on whether seven [eleven] years have passed since the NDA approval without reference to moiety [ingredient], reference product, or similar indicia of an intent to apply the term as broadly as set forth in the Initial Guidance.

We are also concerned that CMS' implementation creates a substantial set of burdens that were not envisioned when the IRA was enacted. For example, CMS' illustrative scenarios included one for which two manufacturers could be identified as a qualifying single-source drug. One of these manufacturers (the NDA/BLA holder) would be the primary manufacturer responsible for participating in the negotiation process, submitting complete and accurate information, and ensuring access to the maximum fair price (MFP). The primary manufacturer would be responsible for securing information that might be in the possession of, or even confidential to, the secondary manufacturer. The secondary manufacturer has no IRA-related obligations, yet its activities or



omissions could place the primary manufacturer in legal jeopardy in the form of substantial fines and penalties.

Manufacturers could not have foreseen the new landscape CMS' definition of a qualifying single source drug has created, and there may be no recourse available to primary manufacturers unable to comply with CMS' IRA requirements without information and other cooperation from secondary manufacturers. Neither the burden to primary manufacturers nor the substantial leverage that a secondary manufacturer might have in negotiating its compliance have been subjected to the notice and comment usually required when a significant burden is imposed on stakeholders. In fact, CMS did not acknowledge or discuss what, if any recourse it envisions would be available to primary manufacturers in its Initial Guidance.

We urge CMS to reconsider its approach in advance of any legal challenges that might be asserted by manufacturers concerned that they have legal obligations with which they are logistically unable to comply. As noted above, we are concerned primarily with the uncertainty accompanying legal challenges to the implementation of laws designed to benefit patients. This is especially important if CMS' implementation of the new Part D out-of-pocket cost refinements is contingent upon moving forward with the IRA drug price negotiation program, and we ask that CMS inform the patient community that this is not the case.

Conclusion

Once again, we appreciate the opportunity to contribute the perspectives of those within the CLL/SLL patient and caregiver community as CMS implements the drug price negotiation provisions of the IRA. We strongly urge the Agency to expand the window for stakeholder feedback on this important and complex step toward drug selection and negotiation. The patient community has not had sufficient time to determine how the Initial Guidance changes incentives and disincentives, or whether it is more likely to benefit or harm patients. We look forward to a continuing dialogue throughout the IRA implementation process and welcome the opportunity to discuss our comments or the experience of CLL/SLL patients generally.

Thank you for your consideration of these comments. If you have any questions, please feel free to contact me or Saira Sultan, CLL Society's Healthcare Advocacy & Policy Consultant, via email at saira.sultan@connect4strategies.com.

Sincerely,

Brian Koffman, MDCM, MEd

Co-Founder, Chief Medical Officer, & Executive Vice President
CLL Society



April 11, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRARebateandNegotiation@cms.hhs.gov

RE: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure,

Cogent Biosciences, Inc. (“we” or “Cogent”) appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

We are a publicly-traded biotechnology company formed in late 2020 that is focused on developing small-molecule precision therapies for genetically defined diseases. Our approach is to design rational, small-molecule precision therapies that treat the underlying cause of disease and improve the lives of patients. Our most advanced program is bezuclastinib, a small-molecule selective tyrosine kinase inhibitor designed to target exon 17 mutations found within the KIT receptor tyrosine kinase, including KIT D816V. We are currently running three global clinical trials to investigate bezuclastinib in patients with two types of Systemic Mastocytosis, Advanced Systemic Mastocytosis and Non-Advanced Systemic Mastocytosis (together, “SM”), and Gastrointestinal Stromal Tumors, a type of cancer with strong dependence on oncogenic KIT signaling (“GIST”). The FDA has granted orphan drug designation to bezuclastinib for the treatment of both SM and GIST. In addition to bezuclastinib, we formed the Cogent Research Team in 2021 and are developing a portfolio of novel targeted therapies to help patients fighting other serious, genetically driven diseases. Our corporate headquarters are located in Waltham, Massachusetts, and our Research Team is located in Boulder, Colorado. We employ approximately 150 individuals across these two locations. We are a development-stage company without any approved products, and we rely on outside investment from institutional investors to fund our development efforts. Most recently, in June 2022, we announced positive initial clinical



data from our APEX clinical trial evaluating bezuclastinib in patients with Advanced Systemic Mastocytosis, and we raised \$161.9 million in net proceeds to help fund the continued development of bezuclastinib. Our current cash runway is expected to fund our operations into 2025, and we will continue to rely heavily on additional outside investment before any prospect of having an approved therapy that could potentially generate revenue. With this in mind, we are significantly concerned by the proposed treatment of NDA-path drugs in the Inflation Reduction Act (“IRA”).

While bezuclastinib would likely be an orphan-exempted small molecule under the IRA, we empathize with our peers at other companies who are working on small molecules that the IRA just made far less attractive to investors. Moreover, the IRA has made any small molecule drug candidates that our Research Team discovers and develops in the future significantly less attractive to investors. It would have been our hope that bezuclastinib, should it ever reach the market, would potentially be combined or sequenced with those other medicines to meaningfully roll back and maybe even cure SM and GIST. We note that there are programs in development, including those earlier in our own pipeline, that might have to choose between development for our orphan indication or another, and the IRA requires them to unfortunately choose instead of developing their drugs to their full potential. We are fortunate that biologics managed to retain 13 years of market-based pricing before having their price impacted by Medicare negotiation (which also spills over into Medicaid), and we urge CMS to reduce the prices of small molecule drugs during the 9-13 year period only as little as required by IRA. Wherever it may be possible to interpret the IRA in such a way as to exempt a small molecule from the IRA, we hope that CMS will.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact me by e-mail at andrew.robbsins@cogentbio.com if you have any questions regarding our comments.

Sincerely,

DocuSigned by:

44F928906C38459...

Andrew Robbins
President & CEO



April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Dear Administrator Brooks-LaSure,

Consumer Action for a Strong Economy (CASE) writes today to ensure that the millions of U.S. consumers we represent are heard by urging the Centers for Medicare and Medicaid Services (CMS) to reconsider its initial implementation guidance for the Inflation Reduction Act (IRA).

CASE has been clear from the beginning on the IRA: the prescription drug price controls that this law implements through Medicare “negotiations” could torpedo the incentives for investment into research and development (R&D) for future lifesaving cures. In fact, the law already has. Many important projects have shut down because of the terrible effect that the law’s drug pricing provisions have on R&D.

The initial IRA implementation guidance put forward by CMS does American patients no favors and does not address this fundamental issue with the law. The dangers the IRA poses to future cures and treatments would only be heightened by the disastrous approach taken by this guidance.

The guidance worsens the uncertainty around drug development already created by the IRA. For example, the guidance essentially declares war on our patent system in its proposed implementation of drug price controls. The guidance targets and punishes selected drugs that have longer periods of patent protection left by proposing “adjusting the preliminary price downward.”

Consider the effect that this will have on American intellectual property (IP) protections broadly. Strong IP protections help drive innovation because they incentivize investment in R&D. If you take away that incentive, medical advances could stall. Why invest billions when the government is threatening to step in and thwart any hope for a return on that investment? The damage this could do, especially to post-approval research on existing drugs, is appalling.

This is no surprise. Bad laws like the IRA come about when Americans are not heard by their government. Policymaking in the United States is supposed to be an open process that considers various interests. Instead, this CMS guidance is doubling down on a closed-off, opaque approach. For this initial guidance, CMS only allowed a 30-day comment period to take input from stakeholders. Likewise, CMS is proposing extremely limited avenues for the public to provide input and receive transparency in the selection of drugs considered for price “negotiation.”

CASE urgently requests that the interests of all Americans be considered in the implementation of the IRA’s drug pricing scheme. Do not blaze ahead on implementing this radical agenda while denying patients, consumers, innovators, doctors, and taxpayers their voice.

Sincerely,

Consumer Action for a Strong Economy (CASE)

Consumer Action for a Strong Economy
1800 Diagonal Road, Suite 600
Alexandria, VA 22314
@CASE_forAmerica



April 14, 2023

Meena Seshamani, M.D., Ph.D.
Deputy Administrator and Director of the Center for Medicare
Center for Medicare & Medicaid Services
7500 Security Blvd.
Baltimore, MD 21244

RE: Medicare Drug Price Negotiation Program Guidance

Submitted electronically to IRAREbateandNegotiation@cms.hhs.gov

Dear Dr. Seshamani:

Thank you for the opportunity to provide comments on the March 15, 2023 memorandum entitled "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments."

The Council for Affordable Health Coverage (CAHC) has long supported reduced drug costs, greater access to drug therapies and fostering innovation to help treat and cure disease. CAHC (www.cahc.net) is a broad-based alliance with a primary focus: bringing down the cost of health care for all Americans. Our members include employers, medical providers, patient groups, insurers, agents and brokers, technology companies, pharmaceutical manufacturers, and pharmacy benefit managers who collectively represent tens of millions of lives in the private market.

We are submitting comments on two aspects of the Initial Memorandum:

1. The process CMS is using to implement the program is opaque and lacks critical stakeholder input to ensure the principles of good government are followed. This must be improved.
2. The provisions related to Orphan products must be modified to ensure implementation of the Medicare negotiation program does not harm our most vulnerable patients.

Process

While most businesses are seeking to provide more transparency and accountability for their constituents, the Administration's implementation of the Inflation Reduction Act (IRA) moves in the opposite direction. Under Section 1198 of the Inflation Reduction Act, Congress instructed HHS to implement the negotiation law by "program instruction or other forms of program guidance" for 2026, 2027 and 2028. Congress also limited administrative and judicial review.

This is not the regular process established by Congress to encourage citizen participation in a transparent government for the people.

Enacted in 1946, the Administrative Procedures Act ensures citizens have a right to be heard by government, that government responds to their concerns, and that parties harmed by government have access to recourse. The law includes requirements for informing the public of rules and providing for public participation in the rule making process by publishing notices of proposed and final rulemaking in the Federal Register and the opportunity for the public to comment on notices of proposed rulemaking.

While CMS must produce the program guidance as instructed, CMS was not instructed by Congress on the process for seeking out and responding to stakeholder input. We are disappointed that CMS has solicited feedback in limited venues, on limited sections of the law, from a discrete panel of stakeholders who already support the program. A law of this magnitude and complexity should have robust stakeholder feedback, including diverse views from every party impacted. We are concerned to learn that some stakeholders have been told their comments may not even be read, much less responded to.

Additionally, the inclusion of language that bars manufacturers from being transparent about government activities during the negotiation process is an egregious overreach of government censorship. CMS proposes a sweeping policy that would restrain manufacturer speech by placing limits on what a manufacturer can use or disclose from CMS offers, requires a “certificate of data destruction” of any and all material related to the negotiation process- including the manufacturer’s own written notes or emails, and prevents manufacturers from audio or video recording any oral conversations between CMS and the manufacturer. This proposal seriously undermines transparency and the ability to validate information if a conflict arises. The need to shield CMS decision-making process from scrutiny will erode public confidence in the price-setting process and should be removed.

Recommendation: We encourage CMS to open the process up to sunshine by:

- **Making your meetings transparent (with recorded minutes and records of attendees) with any stakeholder willing to participate.**
- **Provide responses to stakeholder questions through the program guidance process. Congress provided \$3 billion in funding to implement the program. We suggest spending some of this money on outreach and response to legitimate concerns and questions. CMS is undermining its credibility by failing to respond to stakeholders.**
- **Work with Congress to change the law to require the program be implemented through the regular rulemaking process. While the guidance route may be expeditious for CMS employees, it undermines citizen trust in the program and the Agency itself. There is little reason to continue using program guidance rather than the normal rulemaking process in the program's second or third year.**
- **Remove the gag clause on manufacturers to destroy all information related to the negotiation process.**

There is nothing in law that precludes CMS from having a more transparent, accountable process. We encourage you to open up the process and commit to the responsible implementation of the law.

Orphan Products

More than 10,000 rare diseases impact more than 30 million people (about the population of Texas) in the United States. Fewer than 5% of these diseases have any FDA-approved therapies. Half of those afflicted with a rare disease are children and thirty percent of them will die before their fifth birthday due to the lack of available treatments. For most of the 1 in 10 Americans with a rare disease, surgeries or other medical procedures will not help – they need prescription drugs to either keep their disease from progressing, to get better, or hopefully with new advancements in drug development, be cured. The rare disease ecosystem is extremely sensitive to changes in policy and incentives that drive investment in these patient populations which are high risk and have unmet needs.

Under the IRA, if a chemical drug has been FDA-approved for at least seven years (at least 11 years for a biological product) it may be eligible for price “negotiation.” There are exceptions. For example, drugs with a generic or a biosimilar substitute are exempt from price limits.

The law states that CMS must exclude from price controls a drug “...for only one rare disease or condition and for which the only approved indication (or indications) is for such disease or condition” (Section 1191(e)(3)(A)).

The intent behind this language was to continue to incentivize drug development for rare diseases, carving out products that treat rare diseases from the damage that price controls will cause to access and innovation where it is needed most. However, drug developers often continue research on approved products for other indications and conditions. Particularly in the rare disease community, where studying potential new uses of repurposed products can lead to faster access and less expensive therapies for diseases in need of treatments, this is especially important. More than 60 percent of oncology medications approved more than a decade ago, for example, received additional approvals to treat new indications in later years. Yet under the IRA, if a product indicated to treat one rare disease was studied and approved for the treatment of another rare disease, the product could be subject to price limits, thereby eliminating the incentive to study approved products on additional patient populations and disease groups.

The IRA makes clear that companies developing orphan drugs are now at increased risk of market failure – the opposite of what the Orphan Drug Act sought to address through tax, market exclusivity, and other incentives. Companies are unlikely to invest in products that could be subject to price limits because they are unlikely to see a return on their investment. Stack that negative incentive on top of others that already make this a difficult landscape for drug development – fewer patients (many of them pediatric), high cost of clinical trials, difficulty designing trials that meet the FDA’s demands and regulatory uncertainty – and it makes the market for orphan products very unfavorable. Faced with this uncertainty, investors and manufacturers are unlikely to develop follow-on treatments for the more than 30 million Americans (and their caregivers) who all share the same desire: to have treatments developed for their diseases.

We are concerned that the March 15th guidance language on the single rare disease or condition indication is even more restrictive than what was intended by Congress and will undoubtedly have a damaging impact on development of rare disease drugs. Resolving the problems created by the orphan drug language in the IRA must be done quickly and transparently.

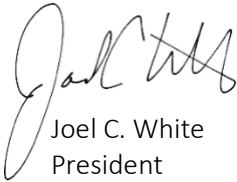
Recommendation: In the program guidance, CMS states the Agency is considering whether there are additional actions it can take to best support orphan drug development. CMS has sufficient flexibility through program guidance in implementing the law to immediately help. Given the limited nature of the exclusion for orphan drugs in the MDPNP, CMS should delay the start of the price negotiation clock for when an excluded orphan product loses its exemption from price controls due to FDA approval of an additional indication until it is proven that the changes do not threaten patient access or innovation. This will help incentivize new research and the discovery of therapies to treat rare diseases. It is pro science and does not conflict with the goal of the law – namely, to reduce prices for products without generic or biosimilar competition.

Conclusion

CAHC encourages CMS to rework the rule to ensure that scientific discovery, product development and patient access are unharmed, and to work with Congress to promote transparency and accountability in rulemaking that will ensure people trust a program of this size and scope is implemented appropriately. While we share your goal of lowering the cost of healthcare, achieving this goal must be approached systemically and not in a way that creates a slew of unintended consequences, namely harming our most vulnerable patients.

If you have questions about these comments, please do not hesitate to contact me.

Sincerely,

A handwritten signature in black ink, appearing to read "Joel White", written in a cursive style.

Joel C. White
President

Council for Affordable Health Coverage



Frank Cullen, Executive Director
Andrei Iancu, Co-Chair
David Kappos, Co-Chair
Judge Paul Michel (Ret.), Board Member
Judge Kathleen O'Malley (Ret.), Board Member

April 14, 2023

Chiquita Brooks-LaSure
CMS Administrator
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and
Director of the Center for Medicare
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Dear Ms. Brooks-LaSure and Dr. Seshamani,

The Council for Innovation Promotion (C4IP) appreciates the opportunity to respond to your March 15, 2023, Solicitation of Comments concerning initial guidance on the Inflation Reduction Act's (IRA) Medicare Drug Negotiation Program.

C4IP is a bipartisan coalition chaired by two former U.S. Patent and Trademark Office directors. We are dedicated to supporting a strong and effective patent system that bolsters U.S. innovation, strengthens our nation's economic competitiveness, and fuels investment in technology that improves lives everywhere.

Unfortunately, several aspects of the Centers for Medicare & Medicaid Services (CMS) guidance would needlessly undermine these goals and devalue the IP protections underpinning life-saving and life-improving innovation.

Section 60.3.4 of the memorandum is particularly concerning in this regard. According to that section, the agency "intends to consider the length of the available patents and exclusivities" when determining the price of medicines under the negotiation program. The agency also notes that "if the selected drug has patents and exclusivities that will last for a number of years, CMS may consider adjusting the preliminary price downward."

In effect, under this guidance, the agency would subjectively lower the initial prices for medicines with longer patents and exclusivities. In so doing, CMS would create a significant disincentive for life sciences firms to perform additional research on medicines already approved by the Food and Drug Administration (FDA), thus impeding continued discoveries that benefit patients.

A great deal of valuable research occurs after a drug's initial FDA approval. During this time, innovators can improve its formula, dosage, and delivery mechanism to reduce side effects and boost treatment adherence. They can also investigate whether a particular medicine has additional applications. In the field of oncology, for instance, it is particularly common to discover that a drug approved for one cancer can treat other forms of the disease. And often, these new indications are only found years after the initial FDA approval.

Under CMS' guidance, however, firms would be penalized for making such progress. If a post-approval discovery yields a new patent or exclusivity, the agency will treat those protections as a reason to devalue a medicine's price further. Once follow-on research becomes a financial liability in this way, companies will lose the asset required to justify the investment of time and resources into these vital ventures. The result will be a significant reduction in the number of medical advances generated by post-approval research.

The precedent established by this guidance would also carry broad consequences for IP-driven innovation in all sectors of the U.S. economy. Virtually every step taken to improve science, manufacturing, or technology is incremental -- and follow-on -- as inventors build on their own progress and the progress of others. For instance, U.S. companies in the high-tech and automotive sectors routinely improve existing products and obtain new patents for these improvements.

The very purpose of patents and other IP protections is to incentivize the disclosure of pathbreaking discoveries so that others can build upon them. The IP system grants researchers and inventors exclusive rights to their creations for a limited period of time. But for IP rights to perform this function, innovators' inventions must be appropriately valued. Otherwise, even the most beneficial innovations would fail to recoup their initial investment costs.

The initial guidance -- and the Medicare Drug Negotiation Program more generally -- would compromise patent-based innovation by empowering the government to devalue the IP rights secured by innovators on a massive scale. A pall of uncertainty would be cast over the entire patent system, weakening the incentives for innovation in a wide range of industries.



Frank Cullen, Executive Director
Andrei Iancu, Co-Chair
David Kappos, Co-Chair
Judge Paul Michel (Ret.), Board Member
Judge Kathleen O'Malley (Ret.), Board Member

We at the Council for Innovation Promotion urge CMS to thoroughly examine the consequences this guidance will have on America's innovative ecosystem, especially on research into the next generation of medicines and technologies.

Thank you again for the opportunity to comment.

Sincerely,

A handwritten signature in black ink, appearing to read 'Frank Cullen', with a long, sweeping horizontal line extending to the right.

Frank Cullen
Executive Director
The Council for Innovation Promotion (C4IP)



April 14, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244–1850

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

The Council of State Bioscience Associations (CSBA) is a coalition of independent state and territory based non-profit trade associations, each of which advocates for public policies that support responsible development and delivery of innovative life-sustaining and life-saving biotechnology solutions. Convened by the Biotechnology Innovation Organization (BIO), CSBA's collective voice represents the true grassroots network of innovators, researchers, manufacturers and accelerators across the country. According to a recent industry report, U.S. bioscience industry employment in 2021 reached 2.1 million jobs in more than 127,000 businesses across every state in the U.S. and Puerto Rico. The total economic impact of the bioscience industry on the U.S. economy, as measured by overall output, totaled \$2.9 trillion dollars in 2021.¹ (TEconomy/BIO, 2022)

The majority of CSBA's member companies are research-intensive small and large biotechnology companies working on cutting-edge innovations. Most of these are pre-revenue human health companies that take enormous risks to develop the next generation of biomedical breakthroughs. Their pipelines have the potential to benefit millions of patients suffering from diseases for which there are no cures or treatments.

We are gravely concerned about the impacts the IRA will have on companies' investments in research and development, as well as the downstream impact on beneficiary access to future treatments and cures. We are especially concerned that treatments for rare diseases, complex medical conditions and those areas with high unmet need will be shelved in favor of treatments that are less likely to be subjected to negotiation.

As such, the CSBA Board of Directors writes today to endorse BIO's formal comments on the Medicare Drug Price Negotiation Program, which are appended to this letter.

¹ TEconomy/Biotechnology Innovation Organization. (2022). *The U.S. Bioscience Industry: Fostering Innovation and Driving America's Economy Forward*. <https://www.bio.org/csba-resources-and-reports>

We look forward to continuing to work with the Agency on these important issues. Should you have any questions, please do not hesitate to contact Michele Oshman, Executive Director for CSBA and Vice President of External Affairs at BIO, at 202-215-8140 or moshman@bio.org.

Sincerely,



Michele Oshman (Apr 14, 2023 10:54 EDT)

Michele M. Oshman
Executive Director, Council of State Bioscience Associations
Vice President, External Affairs
Biotechnology Innovation Organization

Maria Thacker Goethe

Maria Thacker Goethe (Apr 14, 2023 10:57 EDT)

Maria Thacker
Chair, Council of State Bioscience Associations
CEO, Center for Global Health Initiatives and Georgia Bio



John Conrad
Vice Chair, Council of State Bioscience Associations
Illinois Biotechnology Innovation Organization

Attachment:

BIO Comments: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments



Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

April 14, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244–1850

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

The Biotechnology Innovation Organization (BIO) appreciates this opportunity to comment on the initial guidance regarding the Drug Price Negotiation Program (Negotiation Program) under the Inflation Reduction Act of 2022 (IRA) issued by the Centers for Medicare & Medicaid Services (CMS or Agency) on March 15, 2023 (Initial Guidance).¹

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than thirty other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, delay the onset of such diseases, or prevent them in the first place. As a result, our members' novel therapeutics, vaccines, and diagnostics not only have improved health outcomes but also have reduced health care expenditures due to fewer physician office visits, hospitalizations, and surgical interventions. BIO's members include biologic and vaccine manufacturers, which have worked closely with stakeholders across the spectrum, including the public health and patient advocacy communities, to support policies that help ensure access to innovative and life-saving medicines and vaccines for all individuals.

BIO appreciates the steps the agency has taken to establish a dialogue with key stakeholders about the Negotiation Program and other elements of the IRA, but we have significant concerns about the Initial Guidance and the limitations on comments CMS has imposed.

We also believe it's imperative to underscore our views on the IRA. We have long supported a Medicare Part D out-of-pocket cap and the ability for patients to spread these costs throughout the year. These

¹ CMS, Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (Mar. 15, 2023), *available at* <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.



are essential patient protections. At the same time, we believe that patient out-of-pocket costs will never be truly addressed unless the broken rebate system – which benefits pharmacy benefit managers (PBMs) over patients – is addressed. PBMs continue to leverage their size and market influence to ensure they can rake in enormous profits, and they do so at the expense of vulnerable patients.

In addition, we are very concerned about the significant and negative impacts the IRA will have on companies' investments in research and development, which in turn will harm beneficiary access to future treatments and cures, particularly for rare, hard-to-treat diseases and those areas with high unmet need. We continue to urge CMS to consider these impacts as the agency works to update this proposed guidance based on stakeholder feedback.

We also note our strong disappointment that key aspects of this guidance have been issued as final without soliciting comment, which is a concerning step backward from CMS's stated commitment to transparency. BIO strongly urges the Agency to consider stakeholder comments on all aspects of the Initial Guidance. Notably, despite previously committing to "prioritiz[ing] transparency and robust engagement" in its implementation of the Negotiation Program,² the Agency solicits comment on only certain policies, and finalizes other policies with no opportunity for comment—specifically, the foundational policies set forth in Section 30 of the Initial Guidance.³ The Agency's own stated goals of transparency and engagement require immediate reconsideration of this ill-advised start to the Agency's stewardship of the Negotiation Program.

BIO and our members have long argued that the underlying structure of the negotiation program, as set forth by the statute and implemented here by CMS, is legally flawed. In review of the punishing penalties for non-compliance, and the general inflexibility of the process for product selection and maximum fair price (MFP) implementation, these legal flaws cannot be overcome through general guidance clarity at this stage. Nevertheless, we provide herein several suggestions for CMS to consider that might be helpful in the transparency objective of the Agency as it implements this program. None of these resolve the more fundamental legal infirmities of the overall program, nor could they.

We outline below how the implementation of the Negotiation Program would materially benefit from two-sided engagement on all topics, including both a full opportunity for stakeholders to submit comments on proposed policies and meaningful responses to such comments that demonstrate the Agency's consideration of the points made and reveal the reasoning underlying the Agency's final

² CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026 (Jan. 11, 2023), available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf>.

³ While BIO understands that the policies set forth in Section 30 of the Initial Guidance are final and that CMS is not soliciting comment on such policies, BIO sets forth herein for the record the comments that it would have made had CMS solicited comment.



decision-making. Such an approach would fulfill the purpose of a comment period: to enable “[t]he interchange of ideas between the government and its citizenry[, which] provides a broader base for intelligent decision-making and promotes greater responsiveness to the needs of the people.”⁴ The need for such a fulsome process is especially acute here, given the novelty and complexity of the Negotiation Program; the vast ramifications that the program will have for patients, providers, pharmacies, manufacturers, and countless other stakeholders; and the potentially profound negative repercussions for patient access to needed therapies that could follow from errors, misunderstandings, or gaps in understanding. In these circumstances, the Agency should maximize transparency and engagement in its decision-making process, including by both affording a full opportunity for comment and meaningfully responding to stakeholder feedback.

This includes ensuring the negotiation process is transparent, predictable, and fair, with CMS providing necessary accountability to stakeholders and clarifying how it will consider and utilize the broad set of information it will collect and review related to the negotiation factors. Further, we continue to urge CMS to emphasize factors that are critical for patients, specifically factors related to clinical benefit and unmet medical need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.

We also urge CMS to eliminate its proposed, one-sided requirement that manufacturers destroy all records related to the negotiation process and submit a Certificate of Data Destruction to CMS certifying that all information received from CMS during the negotiation period and potential renegotiation period(s) was destroyed. Basic due process mandates that manufacturers be given the ability to maintain records related to negotiation proceedings. Moreover, BIO opposes the blanket prohibition on manufacturers from disclosing or otherwise publicizing information “in the initial offer, including the ceiling price, or the concise justification from the Secretary or any subsequent offer of concise justification, nor information derived from those justifications or offers...”. This one-sided information control heightens the ultimate public complaint that the entirety of the “negotiation” process is anything but actual “negotiation.” BIO disagrees with this approach and recommends CMS abandon it.

We also recommend that CMS finalize the Initial Guidance well in advance of the selected drug publication date for initial price applicability year (IPAY) 2026 to ensure that all stakeholders have ample time before such date to fully digest the contents of the finalized guidance and conform their actions accordingly. Similarly, CMS should solicit comment on proposed guidance applicable to IPAY 2027 and IPAY 2028 (the first IPAY applicable to Medicare Part B drugs) as soon as reasonably possible and well in advance of the selected drug publication dates for such IPAYs.

⁴ *Buschmann v. Schweiker*, 676 F.2d 352, 357 (9th Cir. 1982) (internal quotation marks and citations omitted).



Below please find an overview of our recommendations; our more detailed comments follow.

Regarding the definitions of qualifying single source drugs and negotiation eligible drugs:

- BIO strenuously disagrees with CMS's approach to identifying a qualifying single source drug by reference to common active moiety (drugs) or common active ingredient (biologics). Both law and policy dictate that a qualifying single source drug be identified by reference to its NDA or BLA.
- CMS should clarify the scope of the orphan drug exclusion in a manner that maximizes protections for orphan drugs.
- CMS should take steps to make the process to qualify for the small biotech exception more transparent and predictable.

Regarding the selection, and delayed selection, for negotiation, CMS should:

- Provide for a pre-selection process where, well in advance of the selected drug publication date, CMS would notify each manufacturer of each drug that it intends to select for negotiation and afford each manufacturer a dispute process.
- Improve the process by which a biosimilar manufacturer may request a delay in the selection of a reference product for negotiation due to anticipated biosimilar market entry. This includes providing a meaningful opportunity to request a delay, allowing for a dispute resolution process, and considering all information submitted by a biosimilar manufacturer.

In implementing the negotiation process, CMS should:

- Provide for robust and meaningful engagement and dialogue between the Agency and the manufacturer throughout the negotiation process.
- Allow manufacturers to supplement timely submissions where a post-submission development arises or there otherwise is good cause.
- Provide a meaningful justification of its initial offer and its response to any counteroffer and afford the manufacturer a meaningful opportunity to comment on the response the MFP is set.
- Provide more fulsome safeguards to ensure that the Agency is adequately protecting the confidentiality of all proprietary information submitted to CMS as part of the negotiation process.
- Withdraw its overly broad confidentiality obligations imposed on manufacturers.

In setting the MFP, CMS should:

- Impose on itself bright-line limitations that mitigate the negative effect of the MFP on patient access and on therapeutic innovation.
- Commit to setting the MFP at a price that will not imperil patient access.



- Ensure that the MFP is not set below the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.
- Ensure that the MFP is not set below the MFP ceiling during any year of the price applicability period into which patent protection extends.
- Ensure that the MFP is set at the MFP ceiling until at least the first year during the price applicability period that starts after the date on which the most recently approved indication is thirteen years post-approval.
- Ensure the MFP is not set below the MFP ceiling for vaccines recommended by the Advisory Committee on Immunization Practices (ACIP) at the Centers for Disease Control (CDC).
- Ensure predictable, transparent engagement with manufacturers regarding how the MFP was set.

In utilizing the negotiation factors, CMS should:

- Ensure a transparent, fair, and predictable process.
- Emphasize factors related to clinical benefit and unmet need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.
- Utilize a more robust definition of unmet medical need.
- Clarify how it will evaluate the evidence about alternative treatments by different stakeholders and how different evidence will be considered in setting the MFP.
- Ensure that a robust, comprehensive set of information submitted by manufacturers– with any necessary supplemental material – will be accepted and considered by CMS.
- Allow manufacturers to use reasonable assumptions regarding the information they submit on the manufacturer-specific data.
- Reject approaches that would reduce the preliminary price when a drug has available patents and exclusivities.
- Eliminate reporting and other requirements under the Primary Manufacturer/Secondary Manufacturer Construct.

In establishing the MFP Ceiling, CMS should:

- Abandon its proposal to create a new price point calculated based on the four quarters of a calendar year, and instead simply adopt the existing annual Non-FAMP.
- Establish an exceptions process to account for restatements and anomalies.
- Confirm if the time period for determining whether a selected drug is an extended- or long-monopoly drug runs to the start of the applicable IPAY or the selected drug publication date.
- Calculate the MFP ceiling for Part D drugs exclusive of manufacturer price concessions unless they are passed through at the point of sale.



Regarding the requirement that manufacturers provide access to the MFP, CMS should:

- Finalize its proposal that access to the MFP may be provided through an MFP rebate model.
- Utilize a CMS-established third-party administrator (TPA) or clearinghouse.
- Clarify that the proposed fourteen-day period during which an MFP rebate must be paid runs from the date on which the manufacturer has validated eligibility for the rebate.
- Condition payment of a claim for reimbursement for a unit of a selected drug on the accurate use claims modifiers.
- Finalize its proposals that access to the MFP by Part D beneficiaries at the point of sale will be effectuated through plans, not manufacturers.
- Define the MFP discount using a publicly reported metric, such as wholesale acquisition cost (WAC).
- Simplify its approach for applying the MFP across dosage forms and strengths and address concerns with its proposed methodology.
- Abandon its bona fide marketing standard and instead adopt a standard that consistently designates the MDRP “market date” as both the date on which a generic or biosimilar is marketed and the date on which CMS determines that a generic or biosimilar has been marketed.

In addition, we recommend that CMS:

- Clarify that selected drugs are not subject to an inflation rebate.
- Amend its regulatory definition of “unit” to exclude MFP units from the ASP calculation.
- Proceed with caution on the implementation of CMPs and allow manufacturers a reasonable time period to cure deficiencies before CMPs are imposed.
- Ensure that the text of the Negotiation Program Agreement is made available for public comment at least sixty days in advance of the first selected drug publication date.
- Abandon its “Primary Manufacturer” and “Secondary Manufacturer” construct as part of the Agreement as it is impracticable and has no legal basis.
- Protect beneficiary access to needed therapies, including selected drugs, and implement safeguards to ensure such access.

I. Qualifying Single Source Drugs and Negotiation-Eligible Drugs

A. Background

Section 1192(e) of the Social Security Act (SSA) generally defines “qualifying single source drug” to mean:



- A drug product approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act (FDCA) and marketed pursuant to such approval where at least seven years have elapsed since the date of such approval and there is no approved and marketed generic for such product;⁵ and
- A biological product approved under section 351(a) of the Public Health Services Act (PHSA) and marketed pursuant to such licensure where at least eleven years has elapsed since the date of such licensure and there is no licensed and marketed biosimilar for such product.⁶

The statute provides for certain exclusions from the definition of “qualifying single source drug” — certain orphan drugs,⁷ plasma-derived products,⁸ and certain low Medicare spend drugs.⁹

Section 1192(d) generally defines “negotiation-eligible drug” to mean, with respect to an IPAY:

- Each of the top fifty qualifying single source drugs by Medicare Part D expenditures over a specified twelve-month period; and
- Starting with IPAY 2028, each of the top fifty qualifying single source drugs by Medicare Part B expenditures over a specified twelve-month period.¹⁰

The statute provides for the exclusion of a “small biotech drug” from the definition of “negotiation-eligible drug” for IPAYs 2026, 2027, and 2028.¹¹ Section 1192(d)(2) generally defines “small biotech drug” to mean a qualifying single source drug for which:

- The drug’s 2021 Part B or D expenditures are equal to or less than one percent of all drugs’ 2021 Part B or D expenditures; and
- The drug’s 2021 Part B or D expenditures are equal to or more than eighty percent of its manufacturer’s drugs’ 2021 Part B or D expenditures.¹²

The statute provides for the exclusion of “[a] new formulation, such an extended release formulation” from the definition of “small biotech drug.”¹³

⁵ SSA § 1192(e)(1)(A) (the seven years are counted to the selected drug publication date with respect to the applicable IPAY).

⁶ *Id.* § 1192(e)(1)(B) (the eleven years are counted to the selected drug publication date with respect to the applicable IPAY).

⁷ *Id.* § 1192(e)(3)(A).

⁸ *Id.* § 1192(e)(3)(C).

⁹ *Id.* § 1192(e)(3)(B).

¹⁰ *Id.* § 1192(d)(1).

¹¹ *Id.* § 1192(d)(2). The statute also provides for a Maximum Fair Price (MFP) floor for a “small biotech drug” for IPAYs 2029 and 2030. *Id.* § 1194(d).

¹² *Id.* § 1192(d)(2)(A).

¹³ *Id.* § 1192(d)(C).



B. Distinguishing among qualifying single source drugs and dosage forms and strengths of such drugs

It is imperative that CMS reconsider its approach to identifying a qualifying single source drug and its dosage forms and strengths by reference to common active moiety (drugs) or common active ingredient (biologics), and instead identify such a drug and its dosage forms and strengths by reference to common New Drug Application (NDA) or Biologics License Application (BLA).¹⁴

In the Initial Guidance, CMS states that it will treat products as the same qualifying single source drug where, for drug products, they share the same active moiety or, for biological products, they share the same active ingredient, and the same manufacturer holds all applicable NDAs or BLAs.¹⁵ This policy is irreconcilable with the statute.

The statute requires products to be treated as the same qualifying single source drugs only where they share the same NDA or BLA. This necessarily follows from the plain text of section 1192(e)(1). As set forth above, “qualifying single source drug” is defined for products approved under an NDA by reference to whether seven years has elapsed since “such approval;”¹⁶ likewise, the term is defined for products licensed under a BLA by reference to whether eleven years has elapsed since “such licensure.”¹⁷

Congress’s use of “such license” and “such approval” in the statute is intentional, unambiguous, and must be given effect. Congress used this language to denote that a qualifying single source drug is distinguished by a distinct approval or licensure—i.e., a distinct NDA or BLA. CMS has no authority to rewrite the plain language of the statute by inventing an ultra vires distinction between qualifying single source drugs based on their applications. Where “Congress has been unambiguous, neither the Agency nor [a] court may diverge from that intent.”¹⁸

Although the plain language of the statute is dispositive, BIO notes that other canon of statutory construction confirm Congress’s unambiguous intent to distinguish qualifying single source drugs based on distinct NDAs or BLAs and to mandate that drug and biologic products would not be subject to price controls unless a sufficient time has elapsed since “such approval” (7 years) or “such licensure” (11 years).¹⁹ Of particular note, the statute defines “qualifying single source drug” by express reference to

¹⁴ For a discussion of the related and equally critical concern with CMS’s “bona fide marketing” standard, please see section VI.F.

¹⁵ Initial Guidance at 8.

¹⁶ SSA § 1192(e)(1)(A).

¹⁷ *Id.* § 1192(e)(1)(B).

¹⁸ *Cabazon Band of Mission Indians v. Nat’l Indian Gaming Comm’n*, 827 F. Supp. 26, 29 (D.D.C. 1993), *aff’d*, 14 F.3d 633 (D.C. Cir. 1994).

¹⁹ See *Chevron v. Nat’l Res. Def. Council*, 467 US 837, 843 n.9 (1984) (in addition to the plain text, the traditional tools of statutory construction are used to ascertain the intent of Congress).



the FDCA and PHSA. It is well understood that a statute should be interpreted in the manner “most compatible with the surrounding body of law into which the provision must be integrated.”²⁰

CMS should therefore look to the well-established framework under the FDCA and PHSA for distinguishing among products. Under this framework, drug and biological products generally may be marketed only if approved or licensed by FDA,²¹ and manufacturers seeking such approvals or licensures must meet stringent requirements bearing on safety, effectiveness, and other considerations.²² In implementing this framework, FDA has spoken directly to the circumstances under which a change to an existing product is so significant that it yields a new product warranting a new NDA or BLA is, as well as the circumstances under which a change to an existing product is not.²³ It is manifestly reasonable and appropriate to rely on such FDA standards here, such that a product approved or licensed under a new NDA or BLA is a distinct qualifying single source drug.

There are immeasurable benefits to giving effect to the statute as written and, as Congress intended, adopting FDA’s application-based framework for distinguishing products (as opposed to CMS’s newly invented, statutorily unmoored scheme for doing so). First, and most critically, doing so would avoid exacerbating the disincentive to develop next-generation therapies inherent in the Negotiation Program to the point of suffocating all such innovation, to the detriment of patients in need. The sheer breadth of CMS’s “qualifying single source drug” definition—which amalgamates drug products by common active moiety and biological products by common active ingredient—leaves no incentive for therapeutic advancement and will have significant, negative impacts on innovation for years to come. Biopharmaceutical innovation is incremental, relying on sustained and continuous improvements to molecules, pathways, and modes of administration to achieve maximum clinical benefit for patients. Researchers cannot take significant leaps and develop new active moieties with each generation of treatment. By combining drugs at the active moiety or active ingredient level, CMS is harming investments into new therapies, including for orphan and hard to treat diseases. For the sake of pharmaceutical and biotechnology innovation, and patient access to needed therapies, CMS’s current framework cannot stand.

²⁰ *Green v. Bock Laundry Machine Co.*, 490 U.S. 504, 528 (1989) (Scalia, J., concurring); cf. *Erlenbaugh v. United States*, 409 U.S. 239, 243–44 (1972) (under the rule of *in pari materia*, it is generally “assume[d] that whenever Congress passes a new statute, it acts aware of all previous statutes on the same subject”).

²¹ 21 U.S.C. § 355(a); 42 U.S.C. § 262(a)(1)(A).

²² 21 U.S.C. § 355(c), (d); 21 C.F.R. §§ 314.105, 314.125 (NDA requirements); 42 U.S.C. § 262(a)(2)(C); 21 C.F.R. §§ 601.2(a), 601.4(a) (BLA requirements).

²³ FDA, Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees (Dec. 2004), available at <https://www.fda.gov/media/72397/download>. For example, a new active ingredient (e.g., a different salt, ester, or complex of an approved moiety) should be approved under a new application. *Id.* at 3. In contrast, a new strength generally should be approved under a supplement. *Id.* at 4. The same is true for a new container size or package type of the same indication and route of administration. *Id.* Certain changes in dosage form and route of administration should be approved under a supplement, but others should be approved under a new application. *Id.* at 3.



Second, an application-based framework would create an easily administrable bright line rule based on a familiar standard, to the benefit of both CMS and manufacturers. A bright line rule would enable CMS to more readily identify relevant dosage forms and strengths for purposes of aggregating Medicare expenditures and applying the MFP.²⁴ And a bright line rule would enable manufacturers to more confidently track the seven- or eleven-year “qualifying single source drug” clock, and thereby make more informed decisions about research and development.

For these reasons, BIO strenuously disagrees with CMS’s approach to identifying a qualifying single source drug by reference to common active moiety (drugs) or common active ingredient (biologics). Both law and policy dictate that a qualifying single source drug be identified by reference to its NDA or BLA.

Notably, it necessarily follows from the identification of a qualifying single source drugs by reference to its NDA or BLA that the dosage forms and strengths of such a drug (across which Medicare expenditures are aggregated and the MFP is applied) also must be identified by reference to the NDA or BLA of the drug. With respect to a qualifying single source drug, the statute requires CMS to aggregate Medicare expenditures “us[ing] data that is aggregated across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended release formulation, and not based on the specific formulation or package size or package type of the drug.”²⁵ Similarly, with respect to a qualifying single source drug that is a selected drug, the statute requires CMS to “establish[] . . . procedures to compute and apply the maximum fair prices across different strengths and dosage forms of [the] drug and not based on the specific formulation or package size or package type of such drug.”²⁶ Accordingly, Medicare expenditures are to be aggregated, and the MFP is to be applied, across only dosage forms and strengths of the qualifying single source drug. As set forth above, a qualifying single source drug must be identified by reference to its NDA or BLA; it necessarily follows that the dosage forms and strengths of such a drug also must be identified by reference to the NDA or BLA of the drug.²⁷

It is imperative that CMS immediately rescind the approach set forth in the Initial Guidance—under which Medicare expenditures are aggregated, and the MFP is applied, across dosage forms and

²⁴ See SSA §§ 1192(d)(3)(B), 1196(a)(2).

²⁵ *Id.* § 1192(d)(3)(B) (emphasis added).

²⁶ *Id.* § 1196(a)(2) (emphasis added).

²⁷ The references to “formulations” in the statutory text do not change the analysis. In context, such formulations are plainly limited to formulations of the dosage forms and strengths of the qualifying single source drug. See, e.g., A. Scalia & B. Garner, *Reading law: The interpretation of Legal texts* 199, 203-132–33 (2012) (“[T]he verb to include introduces examples, not an exhaustive list.”). We note that formulations of dosage forms and strengths may be approved under the same NDA or BLA. See FDA, Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees 3–4.



strengths of products that share the same active moiety (drugs) or the same active ingredient (biologics)—and instead specify that, for purposes of aggregation of Medicare expenditures and application of the MFP, dosage forms and strengths are also identified by reference to the NDA or BLA of the qualifying single source drug, consistent with the requirements of the statute.²⁸

C. Orphan drugs

BIO urges CMS to clarify the scope of the orphan drug exclusion in a manner that maximizes protection for orphan drugs.

A drug is categorically ineligible for selection for negotiation if “designated as [an orphan drug] for only one rare disease or condition . . . and . . . the only approved indication (or indications) is for such disease or condition.”²⁹ It is imperative that CMS implement the orphan drug exclusion to be maximally protective of orphan drugs, in recognition of the unique need to maintain incentives for developing new therapies targeting rare diseases.

The Negotiation Program poses special risks to patient populations awaiting the development of new orphan drugs. By definition, orphan drugs target diseases affecting less than 200,000 people in the United States.³⁰ As such, such drugs are particularly susceptible to the chilling effect of factors that discourage research and development. On average, the development of a single drug takes anywhere from ten to fifteen years and costs upwards of \$2.6 billion in research and development³¹—and the development of an orphan drug, often takes even longer and costs even more. Limited patient populations make it inherently more challenging for the developers of orphan drugs to recoup this investment, especially because orphan drug developers are overwhelmingly small emerging companies: Start-ups and emerging biotechnology companies are responsible for fully 85% of all orphan-designated products in development.³²

²⁸ Regardless of the “qualifying single source drug” definition adopted by the Agency, CMS must consistently apply such definition. As such, if CMS were to maintain that products that share the same active moiety (drugs) or the same active ingredient (biologics) are the same qualifying single source drug, BIO agrees that the market entry of a generic or biosimilar to any such product would disqualify all such products from treatment of a qualifying single source drug. See Initial Guidance at 10. Any other approach would be irreconcilable with CMS’s stated “qualifying single source drug” definition. See, e.g., *Nat’l Credit Union Admin. v. First Nat. Bank & Tr. Co.*, 522 U.S. 479, 501–02 (1998) (a basic canon of interpretation is that similar or identical language “be accorded a consistent meaning”).

²⁹ SSA § 1192(e)(3)(A) (such drugs are categorically ineligible for selection for negotiation because they are excluded from the definition of “qualifying single source drug”).

³⁰ See 21 C.F.R. § 316.10(d)(8)(ii).

³¹ T. Sullivan, A Tough Road: Cost to Develop One New Drug Is \$2.6 Billion, Policy & Med., <https://www.policymed.com/2014/12/a-tough-road-cost-to-develop-one-new-drug-is-26-billion-approval-rate-for-drugs-entering-clinical-de.html> (Mar. 21 2019).

³² D. Thomas & C. Wessel, 2019 *Emerging Therapeutic Company Trend Report*, BIO Industry Analysis 40 (2019), available at <http://go.bio.org/rs/490-EHZ-999/images/BIO%202019%20Emerging%20Company%20Trend%20Report.pdf>.



As such, it is vitally important that CMS take special steps to protect development of and access to orphan drugs. The stakes could not be higher for patients. There are over 7,000 known rare diseases, and approximately thirty new ones are identified each year.³³ While each rare disease affects only a relatively small number of patients, collectively, over thirty million Americans are affected by a rare disease, with an estimated cost to society in excess of \$1 trillion annually.³⁴ Further, 95% of rare diseases currently have no approved medical treatment.³⁵ According to a 2020 IQVIA/National Organization for Rare Diseases report examining trends in rare disease innovation, “there are [only] 447 drugs with orphan-only indications, with 104 drugs approved for two or more orphan indications.”³⁶ As such, there is a pressing need to maintain strong incentives for continuing orphan drug development.

Research and development regarding the application of existing therapies to rare diseases is one way to chip away at this disparity. The orphan drug exclusion, however, discourages precisely such scientific discovery. Therefore, as the Agency “consider[s] whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development,”³⁷ BIO urges the Agency to implement, at a minimum, the following recommendations to better support ongoing development of and access to drugs targeting patients living with rare diseases.

First, CMS should establish a process that enables manufacturers to submit evidence that an indication falls within an orphan drug designation to account for situations where CMS is unable to determine eligibility for the orphan drug exclusion based on a review of FDA’s orphan drug databases.

As set forth above, the orphan drug exclusion is based on whether a drug has an orphan drug designation for a single rare disease, and whether its approved indications are for such rare disease.³⁸ In many cases, CMS will be able to readily determine whether a drug meets such

³³ BIO, Rare Diseases & Orphan Drugs, <https://www.bio.org/policy/human-health/rare-diseases-orphan-drugs> (last visited Feb. 28, 2023).

³⁴ S. Garrison, et al., *The Economic Burden of Rare Diseases: Quantifying the Sizeable Collective Burden and Offering Solutions*, Health Affairs Forefront, <https://www.healthaffairs.org/doi/10.1377/forefront.20220128.987667/> (Feb. 1, 2022).

³⁵ Nat’l Insts. of Health, *Delivering Hope for Rare Diseases 1* (Jan. 2022), available at https://ncats.nih.gov/files/NCATS_RareDiseasesFactSheet.pdf.

³⁶ IQVIA, *Orphan Drugs in the United States 7* (Dec. 2020), available at <https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/orphan-drugs-in-the-united-states-rare-disease-innovation-and-cost-trends-through-2019/orphan-drugs-in-the-united-states.pdf>.

³⁷ Initial Guidance at 11.

³⁸ SSA § 1192(e)(3)(A).



criteria using publicly available information. This is because FDA maintains various databases containing relevant information.³⁹

But there are situations where an approved indication falls within the scope of an orphan drug designation but there is no corresponding grant of orphan exclusivity.⁴⁰ In such situations, CMS cannot rely on FDA's databases, as the Agency states in the Initial Guidance it will do,⁴¹ to accurately determine eligibility for the orphan drug exclusion—because those databases principally track orphan exclusivity, rather than orphan drug designation.⁴²

To account for such situations, CMS should create a process that enables manufacturer to provide evidence that an indication falls within an orphan drug designation, where such fact is not ascertainable from FDA databases alone. Acceptable evidence should include written communications with FDA, whether pre- or post-approval. CMS should also establish this process as soon as possible, so that manufacturers can work with FDA and otherwise develop evidence that their drugs are eligible for the orphan drug exclusion, well in advance of the first selected drug publication date.

Second, CMS should confirm that it will determine eligibility for the orphan drug exclusion based on orphan drug designation *at the time of selection*.

Under FDA regulations, a manufacturer may voluntarily withdraw a requested or granted orphan drug designation at any time.⁴³ Where a manufacturer does so, the withdrawal is publicized, and any benefits associated with the designation cease.⁴⁴ Accordingly, when determining eligibility for the orphan drug exclusion, CMS should confirm that it will look only to orphan designation at the time of selection, and will not look to any prior designation that has been withdrawn. Doing so would help avoid improperly narrowing the universe of protected orphan drugs.

³⁹ Such databases include FDA's orphan drug designation/exclusivity database, the drugs@FDA database, and the Approved Drug Products with Therapeutic Equivalence Evaluations publication (Orange Book).

⁴⁰ There are various circumstances where this can arise. For instance, it can occur in certain circumstances where an orphan drug is approved for the same indication as a previously approved drug, but is not clinically superior to the previously approved drug. In such a circumstances, although the indication falls within the scope of the orphan designation, it does not qualify for orphan exclusivity.

⁴¹ Initial Guidance at 11.

⁴² Orphan exclusivity is, in itself, irrelevant for purposes of the orphan drug exclusion. The orphan drug exclusion is unambiguously based on whether all indications of a drug with a single orphan drug designation fall within the scope of that designation. It is therefore immaterial whether the drug also has (or had) orphan exclusivity.

⁴³ 21 C.F.R. § 316.24(d).

⁴⁴ *Id.*



Third, CMS should clarify that, where an orphan drug loses eligibility for the orphan drug exclusion, the seven- or eleven-year “qualified single source drug” clock runs from *the date on which the drug lost eligibility for the exclusion*.

Doing so would help maximize protection for orphan drugs. Absent such clarification, an orphan drug that loses eligibility for the orphan drug exclusion could be virtually immediately subject to selection for negotiation, simply because it was designated as an orphan drug for a second rare disease or an indication was approved for a second rare disease. CMS’s implementation of the orphan drug exclusion would thereby disincentivize progress in rare disease drug development, which is often predicated upon identification of promising new uses of existing therapies. CMS should act to avoid such a result, as it would further disincentivize developers of orphan drugs from investing in treatments for a second rare disease.

Implementing the above recommendations is necessary to mitigate the risk that the Negotiation Program will deter the development of orphan drugs to treat those suffering from rare diseases. It is also fully consistent with long-standing Congressional policy favoring protection of orphan drugs. Such policy dates back to the early 1980s, when Congress enacted the Orphan Drug Act of 1983 to create various incentives to encourage and facilitate the development of new orphan drugs.⁴⁵ In keeping with Congress’s long-held policy of protecting orphan drugs, CMS should make every effort to ensure that it does not hamper orphan drug innovation as it implements the Negotiation Program and its orphan drug exclusion.

D. Small biotech drugs

Under the IRA, a drug is exempt from negotiation for initial price applicability years 2026, 2027, and 2028 if spending on the medicine comprises: (1) a small percentage of Medicare program spending, and (2) a significant proportional share of a company’s Medicare business. This is referred to as the Small Biotech Exception. This critical protection recognizes that small biotech manufacturers with a single product that represents the vast majority of their Medicare revenue will be disproportionately impacted by negotiation, which could have an immediate and tangible impact on the ability of such manufacturers to invest in future R&D – and in particular, in areas that predominantly affect the Medicare population.

CMS does not address how or when it will notify manufacturers regarding its determination of whether a drug, based on the information the manufacturer submits through the proposed ICR, qualifies for the Small Biotech Exception. **To that end, our comments that follow focus on ensuring predictability and**

⁴⁵ See Orphan Drug Act, Pub. L. No. 97-414, §§ 1, 2, 96 Stat. 2049, 2049–51 (1983), as amended by Pub. L. 98-551, 98 Stat. 2815, 2817 (1984).



transparency for small biotech manufacturers that apply for the exception. This includes the following process attributes:

- Clear process (i.e., who submits, what to submit, when to submit) for applying for or recertifying a drug qualifies for the Small Biotech Exception.
- Appropriate and fair timelines to submit information to qualify.
- Consistency and clear criteria in evaluating submissions to qualify for the Small Biotech Exception.
- Proper and timely notification regarding qualification if the drug meets the Small Biotech Exception requirements.
- Proper and timely notification if the drug does NOT meet the Small Biotech Exception requirements, as well as a clear dispute process for appeal of such decision.
- Clarity regarding the form and manner that CMS will use to notify manufacturers if they meet – or do not meet – the criteria for the Small Biotech Exception.

Submissions for Initial Price Applicability Year 2026. CMS has indicated that the current Small Biotech Exception ICR is focused only on initial price applicability year 2026. However, as discussed further below, given that the agency has not made publicly available the data on which it will rely with regard to total expenditures for the purpose of determining eligibility for the Small Biotech Exception under section 1192 (d)(2,) or whether a drug meets the test of a high spend drug under section 1192 (d)(1), it is impossible for small biotech manufacturers to make a reasonable inference regarding whether a submission is warranted in the current or future years on the basis of the requisite statutory thresholds. We recommend that any company that believes it qualifies for the Small Biotech Exception under section 1192 (d)(2) should be able to apply and be approved for this exception this year regardless of whether the drug meets the test of a high spend drug under section 1192 (d)(1). This will provide important certainty and predictability for small biotech manufacturers. Such certainty is critical as most small biotech manufacturers have only one or a limited number of products on the market. We also believe the statute contemplates such an approach, as the exception in section 1192 (d)(2)(A) refers to a “qualifying single source drug” that meets either the test in section 1192 (d)(2)(A)(i) or section 1192 (d)(2)(A)(ii), and these tests refer to Medicare expenditures in 2021, and the data for any small biotech company is readily available to CMS. To provide additional predictability and mitigate uncertainty for small biotech manufacturers, CMS should also clearly articulate the specific criteria manufacturers should consider in determining whether to apply for the Small Biotech Exception for initial price applicability year 2026.

Clarity on Process and CMS Response to Small Biotech Manufacturer. CMS should specify not only the timeline for when the submission of information by the small biotech manufacturer is due, but also the timeline for CMS review and response to the manufacturer, in situations where CMS grants the



exception as well as situations where CMS does not. To promote certainty for small biotech manufacturers, CMS should commit to responding to each manufacturer as far in advance of September 1, 2023, as possible.

- *Clear Timelines.* We suggest the following as a timeline that would allow for appropriate transparency, clarity, and completion of the process in advance of the September 1, 2023, publication of drugs selected for negotiation:
 - Submission by small biotech manufacturers due June 10, 2023;
 - CMS response to small biotech company (affirmative or negative) due by June 30, 2023;
 - Small biotech company response to negative determination by July 20, 2023;
 - Final CMS response to small biotech company by August 10, 2023.
- *Clarity on Data Source for 2021 Drug Spending and Availability of Data for Manufacturers.* CMS should clarify what data source it will use for identifying 2021 total expenditures for the qualifying single source drug, as the agency has stated that the drug dashboard data published at [cms.gov](https://www.cms.gov) is not being used for the IRA negotiation provisions; we also understand CMS is considering use of Prescription Drug Event (PDE) data. We recommend that CMS provide the data it will be using for 2021 to manufacturers so that this data can be validated by manufacturers that apply for (or will apply for) the Small Biotech Exception.
- *CMS Response and Justification for Decision.* CMS should provide clarity on the form and content of its expected response and notification to small biotech manufacturers applying for the exception, specifically whether the response will be by letter, email, or other form of official communication. Further, if CMS determines that it does not agree that a small biotech drug qualifies for the exception, CMS's response should outline in sufficient detail how such a determination was made, including on which expenditure data the agency relied and other information, as relevant, that led to a negative determination. Further, CMS should indicate if the rationale for the denial is restricted to initial price applicability year 2026 or all years for which the Small Biotech Exception applies.
- *Dispute Resolution.* CMS should provide a dispute resolution process where the manufacturer can respond to and appeal a negative determination by CMS. Specifically, the small biotech manufacturer should have the opportunity to provide additional data or information to the agency to support its application for the Small Biotech Exception.
- *Flexibility.* Given that this is a new program and process, and that only a limited number of small biotech manufacturers will be providing submissions to CMS, we recommend that the agency allow for a flexible approach. For example, if CMS determines that information submitted by the



small biotech manufacturer is incomplete or unclear, we urge CMS to engage in a dialogue with the manufacturer to resolve any outstanding issues to complete their submission. Further, for the first year of the program, we encourage CMS to allow a small biotech manufacturer to submit information after the information submission deadline, such as in good faith circumstances where a small biotech manufacturer may later realize that it should qualify for the exception.

- *One-time Qualification.* We request that manufacturers should not need to reapply in subsequent years if a drug has previously received the Small Biotech Exception and there is no material change in the manufacturer's circumstances. Manufacturers could submit an attestation that nothing in their application has materially changed from the prior year and if there has been a material change the manufacturer could submit an updated form.
- *Clear Definition of "Acquired."* We recommend CMS include a definition for what it means to be "acquired" pursuant to section 1192(d)(2)(B)(ii). CMS should consider defining an acquisition as the transfer of substantially all assets of the manufacturer. Further, CMS should specify whether the acquiring manufacturer meeting the definition of a specified manufacturer will be determined at the time of acquisition. If the acquisition results in a change in eligibility for the small biotech exemption, an updated form should be submitted.
- *Confidentiality of Proprietary Information, Publication of Drugs Qualifying for Small Biotech Exception.* As with all other aspects of the data submitted under provisions of the IRA, CMS must fully protect the confidentiality of all proprietary information submitted in relation to this ICR. At the same time, CMS should outline its approach for sharing with the public information regarding the small biotech drugs the agency determines qualify for the exception. Further, BIO recommends that CMS publish a summary list of the small biotech drugs and manufacturers that qualified. Such information will be important for understanding the impact of this IRA provision and provide further certainty to small biotech manufacturers. We believe that more detail on



how or why a specific manufacturer's drug qualified as a small biotech drug should only be released if that manufacturer chooses to do so.

II. Selection, and Delayed Selection, for Negotiation

A. Background

For each IPAY, the statute directs CMS to publish a list of the drugs that have been selected for negotiation (under statutorily specified parameters) by February 1 of the year that is two years before such IPAY.⁴⁶

The statute provides for a delay in the selection of a biologic for negotiation where, among other things, CMS finds that a biosimilar is highly likely to come to market within two years of what otherwise would be the selected drug publication date.⁴⁷ A first year of delay is granted if the following criteria are met:

- The biologic otherwise would be an extended-monopoly drug;⁴⁸
- The biosimilar manufacturer requests the delay before what would otherwise be the selected drug publication date;⁴⁹
- The biosimilar manufacturer submits specified information and documents;⁵⁰
- CMS finds that the biosimilar is highly likely to be licensed and market within two years of what otherwise would be the selected drug publication date;⁵¹ and
- Certain disqualifying circumstances are not present.⁵²

A second year of delay is granted if the following criteria are met:

- The biologic otherwise would remain an extended-monopoly drug;⁵³
- The biosimilar manufacturer requests the delay before the date that is one year after what would otherwise be the selected drug publication date;⁵⁴ and
- CMS finds that the biosimilar is highly likely to be licensed and marketed within two years of what otherwise would be the selected drug publication date and that, based on clear and

⁴⁶ SSA §§ 1191(b)(3), 1192(a); *see also id.* § 1191(d)(1) (September 1, 2023, for IPAY 2026).

⁴⁷ *Id.* § 1192(f).

⁴⁸ *Id.* § 1192(f)(1)(A); *see also id.* § 1194(c)(4) (defining "extended-monopoly drug").

⁴⁹ *Id.* § 1192(f)(1)(B)(i)(I).

⁵⁰ *Id.* § 1192(f)(1)(B)(ii).

⁵¹ *Id.* § 1192(f)(2)(A).

⁵² *Id.* § 1192(f)(2)(D)(iii), (iv).

⁵³ *Id.* § 1192(f)(2)(D)(ii).

⁵⁴ *Id.* § 1192(f)(1)(B)(i)(II).



convincing evidence, the biosimilar manufacturer has made substantial progress toward licensure and marketing;⁵⁵ and

- Certain disqualifying circumstances are not present.⁵⁶

Where a second year of delay is not granted or the biosimilar does not come to market within two years of what otherwise would be the selected drug publication date, the biologic is selected for negotiation, and the biologic manufacturer must pay a specified rebate.⁵⁷

B. Pre-selection process

Well in advance of the selected drug publication date, CMS should notify each manufacturer of each drug that it intends to select for negotiation and afford each such manufacturer a reasonable opportunity to dispute the propriety of each such intended selection.

The process for selecting a drug for negotiation is complex. Eligibility for selection is based on multiple factors, including whether a sufficient number of years have elapsed since approval or licensure;⁵⁸ whether a generic or biosimilar has come to market;⁵⁹ whether the drug is eligible for the orphan drug exclusion;⁶⁰ whether the drug is a plasma-derived product;⁶¹ whether the drug is a small biotech drug;⁶² whether Medicare expenditures are sufficiently low to disqualify the drug from selection;⁶³ and whether Medicare expenditures are sufficiently high to qualify the drug for selection.⁶⁴

The intricate nature of the selection process presents an inherent risk of a selection error. Notably, if a selection error were identified after the selected drug publication date, CMS would de-select the erroneously selected drug but could not select a substitute. By statute, for a given IPAY, all drugs must be selected by February 1 of the year that is two years before the IPAY.⁶⁵

CMS can readily mitigate this concern by adopting a process for soliciting feedback from manufacturers of potential selected drugs before the selected drug publication date. Specifically, CMS should provide notice to each such manufacturer at least thirty days in advance of the selected drug publication date.

⁵⁵ *Id.* § 1192(f)(2)(B)(i), (iii).

⁵⁶ *Id.* § 1192(f)(2)(D)(iii), (iv).

⁵⁷ *Id.* § 1192(f)(2)(B)(ii), (C).

⁵⁸ *Id.* § 1192(e)(1).

⁵⁹ *Id.*

⁶⁰ *Id.* § 1192(e)(3)(A).

⁶¹ *Id.* § 1192(e)(3)(C).

⁶² *Id.* § 1192(d)(2).

⁶³ *Id.* § 1192(e)(3)(B).

⁶⁴ *Id.* § 1192(d)(1).

⁶⁵ *Id.* §§ 1192(e), 1192(a); see also *id.* § 1191(d)(1) (September 1, 2023, for IPAY 2026).



CMS should then afford the manufacturer at least fourteen days to identify to the Agency any basis on which the manufacturer believes the drug is not, in fact, eligible for selection. Such a pre-selection process would serve an important role in identifying selection errors and further the Agency's interests in transparency, efficiency, and informed decision-making.

In addition to providing advance notice to each manufacturer of a drug that the Agency intends to select, CMS should provide advance notice to each manufacturer of at least each of the next five drugs that would be selected if one or more drugs that the Agency intends to select were found to be ineligible for selection. Doing so would promote efficiency by giving each such manufacturer the same opportunity to engage with the Agency regarding potential selection errors. And doing so would impose no additional burden on the Agency because CMS is already required to identify the top fifty qualifying single source drugs by Part D expenditures and, starting with IPAY 2028, the top fifty qualifying single source drugs by Part B expenditures.⁶⁶

In addition, in advance of the deadline by which a biosimilar manufacturer must request a delay in the selection of a reference biologic for negotiation, CMS should enable such biosimilar manufacturer to ascertain whether the reference biologic is among the drugs that the Agency intends to select (or one of at least the next five drugs in line for selection).

As set forth above, a biosimilar manufacturer may request a delay in the selection of a reference biologic for negotiation.⁶⁷ By statute, such a request must be submitted before the selected drug publication date.⁶⁸ This requirement results in a fundamental timing conundrum: A biosimilar manufacturer will not know whether it should request a delay until after the deadline for requesting the delays has passed.

CMS tacitly acknowledges this timing conundrum in the Initial Guidance but fails to meaningfully address it. The Initial Guidance provides only that a biosimilar manufacturer that “think[s]” that a reference biologic “may” be selected for negotiation should submit a delay request.⁶⁹ This approach is inadequate. Requiring a biosimilar manufacturer to guess whether to submit a delay request is deeply inefficient and unreasonable; just as “[i]t is one thing to expect regulated parties to conform their conduct to an agency’s [actions] once the agency announces them; it is quite another to require regulated parties to divine the agency’s [actions] in advance.”⁷⁰

⁶⁶ See *id.* § 1192(d)(1).

⁶⁷ *Id.* § 1192(f).

⁶⁸ *Id.* § 1192(f)(1)(B)(i).

⁶⁹ Initial Guidance at 16.

⁷⁰ *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 158–59 (2012).



To make the delay request provision meaningful, it is essential that CMS instead create a way for a biosimilar manufacturer, with appropriate confidentiality safeguards, to ascertain whether a reference biologic is likely to be selected before the delay request submission deadline. CMS should enable a biosimilar manufacturer to inquire with the Agency starting at least thirty days in advance of such deadline.

C. Delayed selection of a biologic for negotiation on account of anticipated biosimilar market entry

As set forth below, BIO makes a number of recommendations to enhance the implementation of the process by which a biosimilar manufacturers may request a delay in the selection of a reference product for negotiation.

As set forth above, the statute directs CMS to delay the selection of a biologic for negotiation under specified circumstances.⁷¹ BIO makes the following recommendations to enhance the implementation of the delay process:

First, it is vital that CMS afford a biosimilar manufacturer a *meaningful* opportunity to request a delay, reset the delay request submission deadline closer to the selected drug publication date and permit broad supplementation of a timely request.

If CMS does not adopt these recommendations, it will undermine the fidelity of the information on which it relies in making a “high likelihood” determination—and indeed Congress’s objective in providing for a delay request.

With respect to the timing of a delay request, under the Initial Guidance, a biosimilar manufacturer must give notice of its intent to submit a delay request by May 10, 2023.⁷² CMS will then provide a fillable template to complete and access to a Box folder within five business days, i.e., by May 17, 2023.⁷³ The manufacturer must then upload a completed templated and all supporting documentation by May 22, 2023—only three business days later, yet over three months in advance of the selected drug publication date.⁷⁴ There is no justification for such an extraordinarily and needlessly truncated window of time in which to submit a multifactorial request—a concern that is only compounded by CMS’s policy of automatically denying an

⁷¹ SSA § 1192(f).

⁷² Initial Guidance at 21.

⁷³ *Id.*

⁷⁴ *Id.*



incomplete request.⁷⁵ Indeed, such timing constraint works to defeat the Congressional objective in providing for a delay request: By effectively eliminating the additional runway for a biosimilar competitor to come to market, it acts as a barrier to the biosimilar competition that Congress sought to nurture. It is imperative that CMS afford a biosimilar manufacturer a meaningful opportunity to request a delay.

In addition, to ensure that CMS adjudicates a delay request based on the most mature information possible, CMS should (1) set the delay request submission deadline as close as reasonably possible to the selected drug publication date and (2) permit broad supplementation of a timely request with late-breaking information or otherwise for good cause. As noted above, under the Initial Guidance, a biosimilar manufacturer must give notice of its intent to submit a delay request by May 10, 2023—over three months in advance of the selected drug publication date.⁷⁶ And CMS will permit supplementation by the biosimilar manufacturer, beyond supplementation requested by the Agency, only with respect to whether the BLA has been accepted or approved by FDA.⁷⁷

Information bearing on the expected timing of licensure and marketing often rapidly changes. The expected timing of market entry can fluctuate based on a range of factors, including FDA communications regarding the BLA and changes to the manufacturer’s production or distribution arrangements. In order for CMS to make an informed determination regarding eligibility for delayed selection, it is vitally important that the Agency rely on all of the most recent available information that bears on the likelihood of market entry within the requisite time period.

An accurate “high likelihood” determination also reduces administrative burden. If CMS makes an erroneous determination based on outdated or incomplete information, the Agency will be required to administer the payment of a rebate by the reference biologic manufacturer. Such needless inefficiency can be avoided by enabling the Agency to rely on the most recent available information by (1) setting the delay request submission deadline as close as reasonably possible to the selected drug publication date and (2) permitting broad supplementation of a timely request with late-breaking information or otherwise for good cause.

Second, CMS should provide notice of its delay request determination in advance of the selected drug publication date and establish a dispute resolution process.

⁷⁵ *Id.* at 22.

⁷⁶ *Id.* at 21.

⁷⁷ *Id.* at 23.



Under the Initial Guidance, CMS will not inform a biosimilar manufacturer of an unsuccessful delay request until after the selected drug publication date.⁷⁸ This effectively means that the biosimilar manufacturer will have no opportunity to dispute the determination.

The Agency instead should provide notice of an unsuccessful delay request in advance of the selected drug publication date and establish a process by which the biosimilar manufacturer can dispute an erroneous determination. BIO recommends that CMS provide such notice at least fourteen days in advance of the selected drug publication date and afford the biosimilar manufacturer at least seven days to dispute the determination.

Third, CMS should accept and consider all information that the biosimilar manufacturer determines relevant to determining eligibility for delayed selection.⁷⁹

As noted above, there are countless factors that can affect the expected timing of licensure and approval. It follows that CMS should not artificially limit the information that it considers in determining eligibility for delayed selection. Accordingly, it is vital that CMS enable the biosimilar manufacturer—the party closest to the information—to submit all information that it determines relevant to the delay request.⁸⁰

There is clear statutory authority to enable the biosimilar manufacturer to submit such information. The statute provides that the biosimilar manufacturer must submit “information and documents necessary for [CMS] to make [the delayed selection determination], as specified by [CMS]”⁸¹ In addition, the statute provides that, after CMS has reviewed the delay request, the biosimilar manufacturer must submit “any additional information and documents requested by [CMS] necessary to make [the delayed selection determination].”⁸²

CMS therefore has broad discretion in specifying what the biosimilar manufacturer must submit in support of the delay request. The Agency should exercise such discretion and request that the manufacturer submit all relevant information. Doing so would help ensure that CMS has the most pertinent information before it, as the biosimilar manufacturer is the entity best situated to identify the information that bears on the delay request.

⁷⁸ *Id.* at 24.

⁷⁹ See SSA § 1192(f)(1)(B)(ii)(I)(aa) (“information and documents necessary for the Secretary to make determinations under this subsection, as specified by the Secretary”), (II) (“additional information and documents requested by the Secretary necessary to make determinations under this subsection”).

⁸⁰ In the Initial Guidance, CMS enables the submission of only the statutory minimum information. Initial Guidance at 22.

⁸¹ SSA § 1192(f)(1)(B)(ii)(II). The statute goes on to specify that such information “includ[es]” the information specified in section 1192(f)(1)(B)(ii)(III). *Id.*

⁸² *Id.* § 1192(f)(1)(B)(ii)(II).



Notably, CMS also has clear legal authority to consider all such information in making a “high likelihood” determination.

Section 1192(f)(3) sets forth a set of circumstances under which CMS must find a high likelihood of timely market entry—based on a limited set of enumerated information and documents, including information and documents described in section 1192(f)(1)(B)(ii)(III) (subclause (III)).⁸³ Critically, section 1192(f)(3) cannot be interpreted to set forth the only set of circumstances under which CMS may find a high likelihood of timely market entry.

The broader structure of section 1192(f) makes clear that Congress intended that the full range of relevant information and documents be considered by CMS, not only the limited set of information and documents enumerated in section 1192(f)(3). This is because section 1192(f)(1)(B)(ii)(I)(aa) (subclause (I)(aa)) clearly requires the biosimilar manufacturer to submit information and documents necessary to rendering the “high likelihood” determination—“includ[ing]” (but not limited to) the information and documents described in subclause (III).

The necessary implication is that there are information and documents beyond the information and documents described in subclause (III)—which are also “necessary” to rendering the “high likelihood” determination. While the information and documents described in subclause (III) are accounted for in section 1192(f)(3), the remaining information and documents described in subclause (I)(aa) are not—despite being “necessary” to rendering the “high likelihood” determination. Thus, if section 1192(f)(3) were the only set of circumstances under which CMS may find a high likelihood of timely market entry, the language in subclause (I)(aa) requiring broad submission of pertinent information and documents beyond those in subclause (III) would be rendered a nullity.⁸⁴ Because the information and documents described in subclause (I)(aa) serve no other statutory purpose, the only way to give meaning to the entirety of subclause (I)(aa) is to assign it its most natural meaning: Information and documents described in subclause (I)(aa) are “necessary” to rendering the “high likelihood” determination and, thus, CMS may consider all such information and documents submitted in rendering such determination. Accordingly, section 1192(f)(3) does not set forth the only set of circumstances under which CMS may find a high likelihood of timely market entry.

There is every reason to think that Congress intended for CMS to consider all relevant evidence in rendering the “high likelihood” determination. Any other interpretation of the statute would

⁸³ *Id.* § 1192(f)(3).

⁸⁴ See *Duncan v. Walker*, 533 U.S. 167, 175 (2001) (a statute is not to be interpreted in a manner that renders any provision a nullity or otherwise meaningless).



yield an absurd result. Through subclause (I)(aa), Congress clearly granted CMS broad discretion to identify and collect information and documents “necessary” to rendering the determination. If CMS were to refuse to consider such information, it would be tantamount to the Agency acknowledging that it is rendering the determination without considering information and documents that the Agency itself has concluded is essential to doing so. It is hard to imagine more arbitrary and capricious governmental decision-making.⁸⁵ Accordingly, CMS should request all information that a biosimilar manufacturer concludes supports a “high likelihood” determination and consider all such information in rendering such determination.

Fourth, we appreciate CMS’s confirmation that an agreement between a biosimilar manufacturer and a reference biologic manufacturer that permits the biosimilar manufacturer to market the biosimilar is not necessarily an agreement that incentivizes the biosimilar manufacturer to request a delay. But we ask for clarification on the circumstances under which CMS will find a disqualifying agreement to exist.

The statute provides that a delay request may not be granted where, based on specified information,⁸⁶ a biosimilar manufacturer and a reference biologic manufacturer have entered into an agreement that incentivizes (or requires) the biosimilar manufacturer to request a delay.⁸⁷ In the Initial Guidance, CMS correctly acknowledges that an agreement between a biosimilar manufacturer and a reference biologic manufacturer “that permits the Biosimilar Manufacturer to [timely] market the Biosimilar in one or more dosage form(s), strength(s), and indication(s)” not only is not necessarily an agreement that incentivizes the biosimilar manufacturer to request a delay but indeed can be a form of clear and convincing evidence of a high likelihood of timely market entry.⁸⁸ It would be contrary to the statute for CMS to suggest otherwise. This is because the statute clearly directs CMS to consider agreements between the biosimilar manufacturer and the reference biologic manufacturer in rendering the delayed selection determination.⁸⁹ It would nullify this statutory instruction if the mere existence of an agreement between the biosimilar manufacturer and the reference biologic manufacturer were automatically disqualifying. It is well understood that a statute should not be interpreted in a manner that renders text meaningless or otherwise nugatory.⁹⁰

⁸⁵ See 5 U.S.C. § 706(2)(A).

⁸⁶ SSA § 1192(f)(1)(B)(ii)(I)(bb) (“all agreements related to the biosimilar biological product filed with the Federal Trade Commission or the [Department of Justice] pursuant to subsections (a) and (c) of section 1112 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003,” which include agreements between “brand name drug companies” and “generic drug applicants”).

⁸⁷ *Id.* § 1192(f)(2)(D)(iv).

⁸⁸ Initial Guidance at 19.

⁸⁹ SSA § 1192(f)(1)(B)(ii)(I)(bb), (2)(B)(i)(II), (3)(B).

⁹⁰ *United States v. DBB, Inc.*, 180 F.3d 1277, 1285 (11th Cir. 1999) (“A statute should be ‘interpreted so that no words shall be discarded as meaningless, redundant, or mere surplusage.’”) (internal citations omitted).



BIO, however, asks CMS to clarify the circumstances under which the Agency will find a disqualifying agreement to exist. In the Initial Guidance, CMS states only that an agreement may not “impos[e] improper constraints on the Biosimilar Manufacturer.”⁹¹ Yet, despite the absence of meaningful guidance regarding such constraints, CMS will require a biosimilar manufacturer requesting a delay to certify that it has not entered into a disqualifying agreement,⁹² on pain of potential “liability, including under the False Claims Act.”⁹³ To promote market certainty by enabling manufacturers to more confidently make more informed decisions about the arrangements into which they enter, it is imperative that CMS clarify what constitutes an agreement that incentivizes a biosimilar manufacturer to request a delay.

III. Negotiation Process

A. Background

The statute requires CMS to “develop and use a consistent methodology and process” to negotiate the MFP.⁹⁴ In addition, the statute requires the manufacturer to submit specified information by March 1 of the year that is two years before the applicable IPAY.⁹⁵ CMS must make a written initial offer by June 1, which must include a concise justification that considers certain statutorily enumerated negotiation factors.⁹⁶ Within thirty days of receipt, the manufacturer must accept the initial offer or make a written counteroffer, which must include a justification that considers the same statutorily enumerated negotiation factors.⁹⁷ CMS must respond in writing to any counteroffer,⁹⁸ and the negotiation period must end by November 1.⁹⁹

⁹¹ Initial Guidance at 19.

⁹² *Id.* at 77.

⁹³ *Id.* at 80.

⁹⁴ SSA § 1194(b)(1). The renegotiation process must be consistent with the negotiation process to the extent practicable. *Id.* § 1194(f)(1), (4).

⁹⁵ *Id.* §§ 1194(b)(2)(A), (e)(1), 1194(a)(4); *see also id.* § 1191(d)(5)(A) (October 2, 2023, for IPAY 2026).

⁹⁶ *Id.* § 1194(b)(2)(B); *see also id.* § 1191(d)(5)(B) (February 1, 2024, for IPAY 2026).

⁹⁷ *Id.* § 1194(b)(2)(C).

⁹⁸ *Id.* § 1194(b)(2)(D).

⁹⁹ *Id.* § 1194(b)(2)(E); *see also id.* § 1191(d)(5)(C) (August 1, 2024, for IPAY 2026).



B. Negotiation process

BIO asks CMS to adopt its recommendations to improve the proposed negotiation process.

As noted above, the statute mandates that CMS “develop and use a consistent methodology and process” for MFP negotiation.¹⁰⁰ Thus, Congress intended for the negotiation process to be transparent to and predictable for all parties. Although no two negotiations will ever be identical—because the circumstances of each selected drug are unique—all negotiations should be subject to a clear and reasonable framework. A consistent process not only is statutorily required but also helps to ensure that CMS complies with its obligation to treat similarly situated entities in a similar manner, absent a reasoned basis for distinction.¹⁰¹

The Initial Guidance proposes that, only where CMS rejects a counteroffer, the Agency will extend an invitation for a negotiation meeting to take place within thirty days of receipt of such counteroffer.¹⁰² CMS would hold a maximum of three such meetings: an initial meeting and up to one additional meeting at the request of either CMS or the manufacturer.¹⁰³ The Initial Guidance also proposes to allow the parties to discuss new information during such meetings.¹⁰⁴

With respect to justifying an initial offer, the Initial Guidance only recites the statutory requirement of a concise justification based on the statutorily enumerated negotiation factors.¹⁰⁵ The Initial Guidance is silent as to any justification of a response to a counteroffer.

BIO makes the following recommendations to improve the proposed negotiation process:

First, CMS should further enable a negotiation process that allows for meaningful engagement and dialogue between CMS and manufacturers. BIO appreciates that CMS’s recognition that real dialogue (as opposed to a paper-based process) is essential to fulfilling Congress’s intent in establishing a “Negotiation” Program with a mandated process “for negotiations,”¹⁰⁶ which necessarily contemplates meaningful engagement between the Agency and the manufacturer on the unique circumstances presented by each selected drug.¹⁰⁷

¹⁰⁰ *Id.* § 1194(b)(1).

¹⁰¹ See *Bracco Diagnostics*, 963 F. Supp. at 27–28.

¹⁰² Initial Guidance at 55.

¹⁰³ *Id.* at 55–56.

¹⁰⁴ *Id.* at 56.

¹⁰⁵ *Id.* at 54.

¹⁰⁶ SSA § 1194(b)(1).

¹⁰⁷ See *Wheeler v. St. Joseph Hosp.*, 133 Cal. Rptr. 775, 790 (Ct. App. 1976) (differentiating between “negotiated contracts” and contracts of adhesion).



BIO, however, is concerned that the agency is arbitrarily limiting such engagement to (1) the period after the rejection of a counteroffer and (2) a maximum of three meetings. There is no logical reason for such limitations, as (1) such engagement can equally inform an initial offer, potentially sparing the parties the need to consider a counteroffer, and (2) the parties may agree that one or more additional meetings would be helpful and productive in setting the MFP. Accordingly, BIO encourages CMS to revise its proposed negotiation process to (1) enable real dialogue between the parties throughout the negotiation process and (2) specify that, where CMS rejects a counteroffer, additional meetings, beyond those proposed by CMS, may be held without limit where both parties agree to them. We note that such modifications to the negotiation process would be readily manageable given the limited number of drugs subject to such negotiation in any given year.¹⁰⁸

Second, the manufacturer should more generally be permitted to supplement its timely submission where a post-submission development arises or there otherwise is good cause. As set forth above, the statute requires the manufacturer to submit specified information by March 1 of the year that is two years before the applicable IPAY. Inevitably, there will be situations where information relevant to the negotiation arises after the submission deadline has passed. Such late-breaking developments will often be completely unforeseeable at the time of submission but highly relevant to the setting of the MFP. The potential scenarios are virtually limitless: For example, new therapeutic alternatives may come to market; production costs may shift due to ingredient shortages or supply chain issues; or new comparative effectiveness studies may become available.

BIO acknowledges CMS's recognition that it should not blind itself to highly pertinent new information, simply because the submission deadline has passed. But the Agency proposes to limit the presentation of such information to the negotiation meetings during the period after the rejection of a counteroffer. Because such information can equally inform an initial offer, potentially sparing the parties the need to consider a counteroffer, the Agency should more generally permit the manufacturer to supplement its timely submission wherever there is good cause to do so, including when new information relevant to the negotiation process becomes available after the submission deadline.

Permitting supplemental submissions is well warranted. Under the statute, manufacturers are given only one month to prepare a voluminous submission of complex information, including information regarding Non-Federal average manufacturer price (Non-FAMP); research and

¹⁰⁸ See SSA § 1192(a).



development costs; production and distribution costs; federal financial support for discovery and development; pending and approved patent applications, FDA exclusivities, NDAs or BLAs and approvals thereof, market data; and revenue and sales volume data.¹⁰⁹ In some cases, requested data may also not exist in a format required by CMS, such that the manufacturer will need to painstakingly convert raw data from multiple sources into such a format. Manufacturers will assuredly work with utmost diligence to comply with CMS's submission requirements. Still, they may need the flexibility of a supplement to their timely submission for legitimate reasons.

Ultimately, more generally permitting the manufacturer to supplement its timely submission where there is good cause would help ensure that the MFP is set based on the best available information.

Third, CMS should provide a *meaningful* justification of its initial offer and its response to any counteroffer and afford the manufacturer a meaningful opportunity to comment on the response the MFP is set.

As noted above, Congress intended for the MFP to be set via “negotiation,” meaning a bilateral “discussion or process of treaty” between the parties “aimed at reaching an agreement about a particular issue.”¹¹⁰ As with any good faith negotiation, open dialogue will be vital to the success of the MFP negotiation. To this end, BIO asks CMS to specify that its initial offers and its responses to any counteroffers include *meaningful* explanations of how the Agency arrived at the offer or response, including by explaining how the offer or response is supported by the statutorily enumerated negotiation factors and any other information upon which the Agency relied, and how the Agency considered and weighted such factors and information.

As noted above, in the Initial Guidance, CMS states only that the Agency's justification for an initial offer will be “based on” its analysis of statutorily enumerated negotiation factors, but it does not commit to disclosing the details of such analysis.¹¹¹ The Agency does not commit to providing any justification for a response to a counteroffer or an explanation of how it arrived at such response.¹¹²

¹⁰⁹ *Id.* §§ 1193(a)(4), 1194(e)(1).

¹¹⁰ Oxford English Dictionary, Definition of Negotiation, <https://www.oed.com/view/Entry/125879?redirectedFrom=negotiation#eid> (last visited Mar. 2, 2023).

¹¹¹ Initial Guidance at 54.

¹¹² *See id.* at 56–57.



Fully disclosing the bases of both offers and responses to counteroffers would facilitate a more robust—and ultimately more effective—negotiation process. By providing the manufacturer with a meaningful justification for an offer or response, CMS would provide greater opportunity for bilateral dialogue, which would result in more informed and targeted discussions.

BIO also asks CMS to commit to responding to any counteroffer within thirty days. We further ask CMS to commit to affording the manufacturer at least thirty days to comment on the response and considering any such comment before the MFP is set.

This basic procedural protection is essential. Not only would it be consistent with the Agency's stated interest in "prioritiz[ing] transparency and robust engagement,"¹¹³ but it would also result in more informed and accurate decision-making. It would help prevent the MFP from being set based on an error, a misunderstanding, or a gap in information.

There is ample time in the negotiation schedule for such procedural protection. By statute, an initial offer is made by June 1 (February 1, 2024, for IPAY 2026).¹¹⁴ A counteroffer is made within thirty days of receipt.¹¹⁵ Even if CMS were to wait until June 1 (February 1, 2024, for IPAY 2026) to make the initial offer, and even if the manufacturer were to wait until the thirtieth day after receipt make the counteroffer, there would still be four months remaining in the negotiation schedule (five months for IPAY 2026). Thus, there would be ample time for the recommended additional process.

C. Confidential commercial information

BIO acknowledges CMS's stated commitment to confidentiality, but recommends that CMS establish more fulsome safeguards to ensure that the Agency is adequately protecting the confidentiality of all proprietary information submitted to CMS as part of the negotiation process. In addition, BIO opposes CMS's proposed imposition of overly broad confidentiality obligations on manufacturers.

The statute imposes a clear confidentiality requirement: "Information submitted to . . . [CMS] . . . by a manufacturer of a selected drug that is proprietary information of such manufacturer (as determined by . . . [CMS]) shall be used only by . . . [CMS] or disclosed to and used by the Comptroller General of the United States for purposes of carrying out [the Negotiation Program]."¹¹⁶ Congress imposed this

¹¹³ CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026 at 1 (Jan. 1, 2023), available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf>.

¹¹⁴ SSA § 1191(d)(5)(A).

¹¹⁵ *Id.* § 1194(b)(2)(B).

¹¹⁶ *Id.* § 1193(c).



confidentiality requirement for good reason. The statute mandates that manufacturers of selected drugs submit highly sensitive information as part of the negotiation process—including, among other things, information regarding Non-FAMP, research and development costs, production and distribution costs, and revenue and sales volume data.¹¹⁷ It would be deeply disruptive to commercial markets if such proprietary information were disclosed or used in violation of the confidentiality requirement. Indeed, the Initial Guidance acknowledges the “highly sensitive” nature of information to be submitted under the program.¹¹⁸ In principle, BIO is therefore encouraged that CMS states that it “intends to implement a confidentiality policy that is consistent with existing requirements for protecting proprietary information, such as Exemption 4 of [the Freedom of Information Act (FOIA)].”¹¹⁹ That said, there is a pressing need for more detailed specification as to how the Agency will safeguard confidential commercial information to ensure that the statute’s robust confidentiality requirement is fully honored.

BIO therefore asks CMS to more fully specify the controls and safeguards that it will implement. We urge CMS to ensure that such controls and safeguards maximize the protection of confidential commercial information to be submitted under the program. This would be fully consistent with the approach taken in other areas of federal law and policy, which have long given special consideration to such highly sensitive information. For nearly forty years, the Supreme Court has made clear that commercial trade secrets are a “property right [] protected by the Taking Clause of the Fifth Amendment.”¹²⁰ Likewise, Congress has repeatedly made clear its expectation that commercially sensitive information be appropriately safeguarded. For example, even beyond FOIA’s long-standing protection of “trade secrets and commercial or financial information that is obtained from a person and is privileged or confidential,”¹²¹ the Defend Trade Secrets Act prohibits the “misappropriation” of trade secrets through public disclosure and established a private cause of action to enable affected parties to sanction such misappropriation.¹²²

BIO recommends the following minimum controls and safeguards to give full meaning to the confidentiality requirement:

First, CMS should confirm that, in “implement[ing] a confidentiality policy that is consistent with existing requirements for protecting proprietary information,”¹²³ it will ensure protections comparable to, not only those under FOIA, but also those under government price reporting law and policy.

¹¹⁷ *Id.* §§ 1193(a)(4), 1194(e)(1).

¹¹⁸ Initial Guidance at 29.

¹¹⁹ *Id.*

¹²⁰ *Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 1004 (1984).

¹²¹ 5 U.S.C. § 552(b)(4); 45 C.F.R. § 5.31(d).

¹²² 18 U.S.C. § 1839(5)(B)(ii)(II).

¹²³ Initial Guidance at 29.



We appreciate CMS's confirmation that the protections under FOIA, including the prohibition on disclosure of information designated as confidential without providing a pre-disclosure notification and an opportunity to raise objections to disclosure,¹²⁴ will apply to information to be submitted under the program.¹²⁵ We seek confirmation that the protections under government price reporting law and policy will also apply.

In developing the Negotiation Program, Congress did not intend to disrupt the confidentiality requirements under other federal law and policy.¹²⁶ CMS's confidentiality policy should thus maintain the confidentiality of information protected against disclosure under all other federal law and policy. For example, under MDRP, "information disclosed by manufacturers . . . under [MDRP] . . . is confidential and shall not be disclosed by [CMS] . . . in a form which discloses the identity of a specific manufacturer . . . [or] prices charged for drugs by such manufacturer"¹²⁷ Similarly, Medicare Act provides that "[Average Sales Price (ASP)] information disclosed by manufacturers . . . is confidential and shall not be disclosed by [CMS] in a form which discloses the identity of a specific manufacturer . . . or prices charged for drugs or biologicals by such manufacturer"¹²⁸ Likewise, the 340B Drug Pricing Program (340B Program) generally prohibits disclosures of information submitted by manufacturers under the program.¹²⁹ Where confidential commercial information is protected against disclosure under these or any other federal programs, CMS should safeguard such information against disclosure to at least the same extent.

Second, CMS should implement robust storage and access controls and safeguards to protect the confidentiality of sensitive information. Confidentiality requirements are only as meaningful as the data privacy and security protections that are implemented to safeguard sensitive information against inadvertent or malicious¹³⁰ improper disclosure. Accordingly, CMS should implement robust systems and protocols, including by ensuring that all proprietary information stored in the Health Plan Management System (HPMS) and in electronic

¹²⁴ See 45 C.F.R. §§ 5.41, 5.42.

¹²⁵ Initial Guidance at 29.

¹²⁶ See *Nat'l Ass'n of Home Builders v. Defs. of Wildlife*, 551 U.S. 644, 662 2d 467 (2007) ("[R]epeals by implication are not favored" and will not be presumed unless the "intention of the legislature to repeal [is] clear and manifest.").

¹²⁷ SSA § 1927(b)(3)(D) (subject to certain limited exceptions).

¹²⁸ *Id.* § 1847A(f)(2)(D) (subject to certain limited exceptions).

¹²⁹ Health Res. & Servs. Admin., General Instructions for Completing the Pharmaceutical Pricing Agreement 7 (2019), available at www.hrsa.gov/sites/default/files/hrsa/opa/pharmaceutical-pricing-agreement-example.pdf.

¹³⁰ Malicious third-party cyber activities have increasingly targeted the federal government—in, part, because its databases are repositories of significant amounts of sensitive information. Cf. David E. Sanger, *Russian Hackers Broke into Federal Agencies, U.S. Officials Suspect*, N.Y. Times, <https://www.nytimes.com/2020/12/13/us/politics/russian-hackers-us-government-treasury-commerce.html> (last updated May 10, 2021).



communications with the Agency is secure and accessible only to CMS staff and only where there is a legitimate programmatic need for access to such information.

In doing so, CMS should look to the safeguards it has already establish under MDRP. Under MDRP, CMS has implemented a system with numerous privacy and security protections to safeguard sensitive product and pricing data submitted by manufacturers. For example, the online interface allows a manufacturer to view its pricing data, such as its Baseline Average Manufacturer Price (AMP) data, while disallowing states, which do not have a programmatic need to view such information, from doing likewise.¹³¹ CMS should ensure that similar controls are in place with respect to HPMS, given CMS's intent to transition most information submissions to that system.

CMS should also specify how it will maintain the confidentiality of the subset of information that is required to be submitted via e-mail or Box. With respect to e-mail, CMS should explain, among other things, how it will enforce access security controls. With regard to Box (a third-party commercial platform), BIO asks CMS to specify how submitted information will be kept confidential, including as against misuse by Box personnel.

Third, CMS should establish a process to enable manufacturers to review a draft of the explanation of the MFP in advance of its publication and raise concerns about disclosure of confidential information. By statute, CMS is required to publish an explanation of the MFP.¹³² Such publication inherently poses heightened risk of disclosure of confidential commercial information. BIO appreciates that CMS intends to make only high-level comments regarding submitted data and refrain from sharing proprietary information.¹³³ But this is insufficient to safeguard against inadvertent disclosure of confidential commercial information. Accordingly, BIO asks that the manufacturer be given an opportunity to review the intended explanation in advance of publication, as well as an opportunity to raise concerns. Such precaution is well warranted here, given Congress's special emphasis on the need for safeguards with respect to the public explanation of the MFP, as evidenced by its specific cross-reference to the statute's confidentiality requirement.¹³⁴

BIO opposes CMS's proposed imposition of overly broad confidentiality obligations on manufacturers. BIO urges CMS to eliminate the proposed, one-sided requirement that manufacturers destroy all records related to the negotiation process and submit a Certificate of Data Destruction to CMS certifying that all

¹³¹ CMS, *Medicaid Drug Programs User Manual 1* (Nov. 3, 2021).

¹³² SSA § 1195(a)(2).

¹³³ Initial Guidance at 29.

¹³⁴ SSA § 1195(a)(2); see also *id.* § 1193(c).



information received from CMS during the negotiation period and potential renegotiation period(s) was destroyed. Like CMS, manufacturers are responsible for maintaining records associated with material decisions and must do so to maintain proper and adequate lines of supervision and oversight by boards, shareholders, and other stakeholders. Manufacturers must therefore be permitted to maintain (in a confidential format) reasonable records associated with the negotiation process to meet their oversight obligations, just as CMS will be maintaining its own records from the negotiation process.

Further, basic due process mandates that manufacturers be given the ability to maintain records related to negotiation proceedings. As CMS knows, the statute contemplates penalties of up to \$1 million per day for failing to submit required information. CMS's Initial Guidance further specifies that the Agency will consider a manufacturer that knowingly submits false information to have violated this provision. Especially given the vast magnitude of such penalties, it is imperative that manufacturers be permitted to maintain complete records of all information they believe may be relevant to defending against the erroneous imposition of sanctions.

It would be troubling in the extreme if manufacturers were required by CMS to destroy the very records that could one day be needed to defend against penalties that could reach hundreds of millions of dollars. "[T]he essence of due process is fundamental fairness," and little could be more fundamentally unfair than mandating destruction of the very records needed to verify an entity's innocence as against erroneous enforcement.¹³⁵

Moreover, BIO takes issue with the more specific blanket prohibition on manufacturers from disclosing or otherwise publicizing information "in the initial offer, including the ceiling price, or the concise justification from the Secretary or any subsequent offer of concise justification, nor information derived from those justifications or offers...". As with the broader records destruction provisions discussed above, this prohibition amounts to CMS putting its thumb on the scale of transparency as the only entity involved in the negotiation program who can control and confirm information flows. This one-sided information control heightens the ultimate public complaint that the entirety of the "negotiation" process is anything but. Rather, optically – and in practice – it appears CMS is proposing to control the entirety of the negotiation process, and to stifle any outside public discussion of the negotiation process itself. BIO disagrees with this approach and recommends CMS abandon it.

Further, the blanket "gag" sought in the proposed guidance raises several practical and Constitutional concerns. From a broader regulatory standpoint, certain regulatory agencies (*e.g.* The Securities and Exchange Commission) might well have conflicting standards for materiality determinations in disclosures made by publicly traded companies. We would argue that the exclusion in the guidance

¹³⁵ *Evans v. Wilkerson*, 605 F.2d 369, 371 (7th Cir. 1979).



from the disclosure prohibition based on state and federal law might not go far enough in covering certain regulatory obligations – both at the federal and state level. Particularly when considered in context with the records destruction obligations imbued in the guidance as well.

What is more, CMS appears to be making a more general affront to the protected speech of affected manufacturers. As has been reaffirmed many times before, prior restraints on speech are presumptively unconstitutional.¹³⁶ The government faces a heavy burden in showing a compelling interest in keeping negotiation discussions private, and we fail to see a legitimate reason why the government's interests are so advanced by muzzling private companies in the context of Medicare price negotiation discussions.¹³⁷ In fact, in this instance, any potential disclosure by a manufacturer would likely relate to truthful information that is, at a minimum, of significance to at least a portion of the public involved in the transaction of health insurance and health consumption. As such, we recommend CMS abandon these burdensome and unnecessary confidentiality and anti-disclosure provisions.

D. Special considerations in setting the MFP

It is vital that, in setting the MFP, CMS impose on itself bright-line limitations that mitigate the negative effects of the IRA and the MFP on patient access and on therapeutic innovation. BIO strongly urges CMS to adopt the following limitations.

BIO asks CMS to commit to a policy where it will not set the MFP below a price shown to imperil patient access (or otherwise below the MFP ceiling).

It is basic economics that centralized price-setting risks curtailing access to the supply of medicines.¹³⁸ If the government mandates a price too far below the price that would have been set by the free market, there will be an inevitable and profound mismatch between demand and supply.¹³⁹

BIO urges CMS, in carrying out the Negotiation Program, to be attuned to the risk to patient access if the MFP is set unduly low. The stakes are too high for CMS not to give due weight to such risk. The implication of a supply-demand mismatch is not limited to some economist's spreadsheet. Rather, it

¹³⁶ See, e.g., *Near v. Minnesota* 283 U.S. 697 (1931).

¹³⁷ As has been reaffirmed in many instances by the US Supreme Court, the government must articulate a compelling government need for the negotiation to remain out of the public discourse and must simultaneously introduce a narrowly tailored method for so restricting this discussion. In the context of this guidance, we see no such articulation of either a compelling need nor a narrow restriction. In fact, we see just the opposite. See, e.g., *New York Times Co. v. United States*, 403 U.S. 713 (1971).

¹³⁸ S. Atlas, *How to Reduce Prescription Drug Prices: First, Do No Harm*, 117 *Modern Med.* 14, 14 (2020).

¹³⁹ Rent control is the classic Economics 101 illustration: Price controls on rental stock result in undersupply; the result is a net societal loss of utility relative to the pareto optimal price. See, e.g., E. Glaser & E. Luttmer, *The Misallocation of Housing Under Rent Control*, 93 *Am. Econ. Rev.* 1027, 1027 (2003).



could mean the difference between millions of patients having access to life-saving medicines and empty shelves at the pharmacy counter. Indeed, the House Committee on Ways and Means has estimated that loss of innovation due to price controls could result in as many as “42 million patients without the medicine they need.”¹⁴⁰

The risk to longer-term innovation and development of new medicines is even more profound. One recent study by the University of Chicago concluded that the “mid-range effect” of price controls is 254 fewer new drug approvals; the researchers conservatively estimated that the loss in life from the price controls accordingly is twenty times larger than our country’s losses from the COVID-19 pandemic.¹⁴¹ Another study of the European experience found that a “10% drop in the price of medicines in price-controlled [European Union] markets was associated with . . . an 8% increase in the delay of access to medicines.”¹⁴² Still other studies have demonstrated that government price-setting is associated with dramatic declines in early research, which, of course, is the fundamental precursor to a robust and growing pipeline of new therapies targeting areas of unmet medical need.¹⁴³

Therefore, CMS should commit to a policy under which it will not set the MFP below a price shown to further imperil patient access (or otherwise below the MFP ceiling). This approach would help strike an equitable balance, giving weight to the objective of reducing prices today while also mitigating the risk that price controls will significantly imperil the drug supply or further curtail the development of the transformative medicines of tomorrow.

BIO also asks CMS to commit to setting the MFP at the MFP ceiling where failing to do so would further curtail therapeutic innovation.

It is vital that the Negotiation Program strike an appropriate balance such that blunt reductions in Medicare expenditures do not come at the expense of ongoing innovation that yields new and potentially life-saving medicines. Accordingly, BIO urges CMS to commit to setting the MFP at the MFP ceiling where doing otherwise would imperil therapeutic innovation, including in the following circumstances (not exhaustive):

¹⁴⁰ U.S. House Comm. on Ways & Means, Analysis: Americans Don’t Support Surrendering Innovation, <https://waysandmeans.house.gov/analysis-americans-dont-support-surrendering-innovation-for-democrats-drug-price-controls/> (Aug. 4, 2022).

¹⁴¹ See T. Phillipson & T. Durie, The Evidence Base on the Impact of Price Controls on Medical Innovation 1 (2021) (loss in life estimate was over a ten-year time period), available at https://bfi.uchicago.edu/wp-content/uploads/2021/09/BFI_WP_2021-108.pdf.

¹⁴² D. Schulthess & H. Bowen, *The Historical Impact of Price Controls on the Biopharma Industry*, Vital Transformations (Nov. 22, 2021).

¹⁴³ See T. Abbott & J. Vernon, *The Cost of US Pharmaceutical Price Reductions: A Financial Simulation Model of R&D Decisions*, 28 Managerial & Decision Econ. 293 (2007).



First, for a drug (small molecule), the MFP should not be set below the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.

To be selected for negotiation, biologics (large molecules) must be at least eleven years post-licensure, while drugs (small molecules) must be at least seven years post-approval.¹⁴⁴ On account of the approximately two-year time lag between selection for negotiation and application of the MFP, an MFP cannot apply to a biologic until at least approximately thirteen years post-licensure; in contrast, an MFP cannot apply to a drug until at least approximately nine years post-approval. To help preserve small molecule innovation in parity with large molecule innovation, we ask that, for a small molecule, CMS set the MFP at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.

Studies show that most products (whether small or large molecules) achieve modest levels of annual sales in their first five years on the market.¹⁴⁵ Thus, manufacturers may seek the economic benefit of an additional four-year shelter from selection for negotiation by focusing research and development on biologics instead of drugs.

Thus, we ask that CMS act to better balance the incentives regarding small molecule drug and biologic development by setting the MFP for a small molecule drug at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.

Second, the MFP should not be set below the MFP ceiling during any year of the price applicability period into which patent protection extends.

CMS must consider a number of factors in determining the MFP for a selected drug, including “[d]ata on pending and approved patent applications.”¹⁴⁶ We ask CMS to ascertain whether, based on information submitted by the manufacturer, the selected drug will have any remaining patent protection at the start of the price applicability period and, if so, set the MFP at the MFP ceiling price for any year during such period into which such patent protection extends.

¹⁴⁴ SSA § 1192(e)(1).

¹⁴⁵ QuintilesIMS Inst., *Lifetime Trends in Biopharmaceutical Innovation: Recent Evidence and Implications*, at 2 (Jan. 2017).

¹⁴⁶ SSA § 1194(e)(1)(D).



The statute permits a drug to be subject to an MFP nine years post-approval and a biologic to be subject to an MFP thirteen years post-licensure.¹⁴⁷ By the time the price applicability period for a selected drug begins, the product’s regulatory exclusivity period likely will have expired—but not necessarily its patent protection period.¹⁴⁸ In other words, given that a patent protection period can extend beyond a regulatory exclusivity period, it may very well be the case that there will be remaining patent protection for a selected drug that extends into the price applicability period.

In the Initial Guidance, CMS proposes that, if a selected drug “has patents and exclusivities that will last a number of years,” CMS may adjust the “preliminary price” downward.¹⁴⁹ This is the opposite of what the policy should be. A selected drug’s ongoing patent protection supports a higher “preliminary price”—and, indeed, an MFP equal to the MFP ceiling. This is key to supporting pharmaceutical and biotechnology innovation in developing drugs and biologics that treat serious diseases.

It is a long and expensive process to bring a chemical or biological product from research and development to market, and many candidates do not make it through the process. To encourage innovation by rewarding manufacturers for their research and development investments and efforts, the federal government awards pharmaceutical and biotechnology companies with patent protection for a specified period of time. The patent protection period affords a manufacturer the opportunity to recover its research and development costs—not only for the drug for which the patent was awarded but also for other research and development investments that the manufacturer made. To support continued innovation, CMS should honor any remaining patent protection for a selected drug by specifying that the MFP will be set at the MFP ceiling during any year of the price applicability period into which such patent protection extends.

Third, the MFP should be set at the MFP ceiling until at least the first year during the price applicability period that starts after the date on which the most recently approved indication is thirteen years post-approval.

Innovation should not end with the approval of a first indication. Rather, finding novel uses for existing therapies is “essential for maximizing medicines’ therapeutic utility.”¹⁵⁰ Developers of

¹⁴⁷ *Id.* § 1192(e)(1).

¹⁴⁸ See FDA, Frequently Asked Questions on Patents and Exclusivity, available [here](#) (last accessed Mar. 2023).

¹⁴⁹ Initial Guidance at 53.

¹⁵⁰ B. Sahragardjoonegani et al., Repurposing existing drugs for new uses: A cohort study of the frequency of FDA-granted new indication exclusivities since 1997, 14 J. of Pharmaceutical Policy & Practice 1 (2021).



drugs and biologics therefore devote countless hours and untold capital to research and development of new indications, thereby expanding treatments to additional disease states and patient populations.¹⁵¹

In recent years, new indications have spurred vital medical breakthroughs across countless critical medical conditions. For example, new indications have been vital “to increase the portfolio of available effective cancer chemotherapeutic agents for patients.”¹⁵² Similarly, the repurposing of existing therapies has played a critical role in meeting the otherwise unmet needs of patients with rare medical conditions.¹⁵³

The seven- and eleven-year selection clocks work to extinguish such innovation by actively disincentivizing a manufacturer from making the considerable investment necessary to obtain approval of a new indication, given that such indication would run on the same selection clock. CMS must act to mitigate this concern by committing to setting the MFP at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the most recently approved indication is thirteen years post-approval. Such limitation on the setting of the MFP would provide greater certainty to manufacturers as they consider ongoing investment in research and development of new indications. This could avoid wholesale extinguishment of therapeutic innovation, to the detriment of patients with serious unmet medical needs, on account of the seven- and eleven-year selection clocks.

Fourth, the MFP should not be set below the MFP ceiling for vaccines recommended by the Advisory Committee on Immunization Practices (ACIP) at the Centers for Disease Control (CDC). Vaccination is often cited among the 10 greatest public health achievements of the century. In addition to their societal benefit, vaccines deliver significant benefit to individuals throughout their lifetime and allow older individuals to remain healthier and productive in their later years of life. The importance of vaccines was recognized in the IRA, which eliminated cost sharing for vaccines in Medicare Part D, building on the precedent in Medicare Part B where there was no cost sharing for vaccines. Because of the high value that vaccines confer not only to Medicare beneficiaries but to society as a whole, the MFP for vaccines recommended by the ACIP should not be set below the MPF ceiling.

¹⁵¹ See *id.* at 1–2 (noting the significant time and cost associated with obtaining approval of a new indication).

¹⁵² S. Islam, et al., Repurposing existing therapeutics, its importance in oncology drug development: Kinases as a potential target, 88 Br. J. Clin. Pharmacol. 64 (2021).

¹⁵³ See P. Ayyar et al., Repurposing – second life for drugs, 69 Pharmacia 51, 52 (2022).



IV. Negotiation Factors

For purposes of negotiation of the MFP, the statute (SSA 1194 (e)) directs CMS to consider the following factors:

- Manufacturer-specific data (SSA 1194 (e)(1)): Research and development costs and the extent to which the manufacturer has recouped such costs; current unit costs of production and distribution; prior federal financial support for discovery and development; and data on pending and approved patents and exclusivity; and market data and revenue and sales volume data.
- Evidence about alternative treatments (SSA 1194 (e)(2)): the extent to which the drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such alternative; FDA-approved prescribing information for the drug and the alternatives; comparative effectiveness of the drug and the alternatives, including effects on specific patient populations; the extent to which the drug and the alternatives address unmet medical need.

The statute also directs CMS not to use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

A. **Evidence on therapeutic alternatives and unmet need**

CMS should emphasize factors related to clinical value and unmet need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.

In developing a starting point for the initial offer, CMS proposes to utilize the net price for identified therapeutic alternatives and then adjust this starting point based on the review of the clinical evidence to develop a “preliminary price.” CMS will then consider the manufacturer specific data under section 1194(e)(2) and may adjust the preliminary price upward or downward. When there is no therapeutic alternative CMS would adjust the starting point based on how the selected drug fills an unmet medical need.

The proposed approach outlined by CMS is vague, and CMS’s intent is unclear. We strongly support an approach that emphasizes factors related to clinical benefit and unmet medical need and de-emphasizes manufacturer specific data elements such as cost of production and research and development costs – CMS should clarify how it will weight these factors in that regard. CMS should consider and prioritize high quality, robust real-world evidence (RWE), evidence provided by clinicians with the necessary expertise, as well as evidence submitted by manufacturers – who have a vast depth and breadth of



clinical and scientific expertise regarding their marketed therapies. CMS should also focus on patient-centered outcomes and the broader societal benefit conferred by a therapy. Further, providing higher relative MFPs to products that have advanced patient care and address unmet medical need will help maintain investment in assets and clinical programs that show scientific promise. At the same time, it is critical that CMS is transparent in its approach in determining therapeutic alternatives to selected drugs and provides a strong justification that the identified therapeutic alternatives are appropriate and are primarily driven by clinical guidelines and patient need versus cost.

It is essential that CMS clarify how it will evaluate the evidence it receives from different stakeholders and how such evidence will be considered in identifying therapeutic alternatives and setting the MFP.

CMS says it would adjust the preliminary price based on the totality of the relevant information and evidence submitted and gathered through the agency's analysis based on the clinical benefit the selected drug provides compared to its identified therapeutic alternatives. We support an approach that considers a wide range of high quality, robust evidence, including RWE. Further, information submitted by manufacturers should be considered a high priority in CMS's review as manufacturers have deep and unique expertise in their therapeutic areas of focus.

CMS should be transparent and provide sufficient detail regarding its framework for how different evidence was used to inform the identification of therapeutic alternatives for a selected drug, as well as the establishment of the preliminary price as well as the initial offer and response to any counteroffer, including what evidence was most impactful in CMS' analysis and why. CMS' review of the evidence should be patient-centered and have a focus on health equity and reducing disparities. To that end, we strongly support CMS's confirmation that evidence that uses discriminatory approaches such as QALYs will not be considered. We also note that other measures that have been often promoted as alternatives to QALYs – such as the Equal Value of Life Years Gained (evLYG) – are also problematic as they limit the value of interventions that both extend life and improve the quality of life – and CMS should similarly reject them. In reviewing the evidence CMS should recognize both the current and future value of therapies and remain flexible to keep pace with innovations in science and technology. Further, evidence on a therapy should be viewed in the context of its benefits to the Medicare program, as well as the overall health care system.

We recommend that CMS provide manufacturers with robust detail regarding its analysis of evidence throughout the negotiation process and provide manufacturers with opportunities for discussion and dialogue, including before CMS's initial offer in February 2024 and in its identification of therapeutic alternatives that will be used in setting the MFO. CMS should also provide a line of sight into its assessment of the evidence for the broader stakeholder community, so as to ensure appropriate



transparency and accountability not just to manufacturers but to Medicare beneficiaries and to providers and other key stakeholders.

We are concerned that CMS’s proposed definition of unmet medical need is too limiting; the agency should use a more robust definition. We recommend that CMS look to the FDA’s definition outlined in its “Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics.”¹⁵⁴ Under the FDA guidance, “An unmet medical need is a condition whose treatment or diagnosis is not addressed adequately by available therapy. An unmet medical need includes an immediate need for a defined population (i.e., to treat a serious condition with no or limited treatment) or a longer-term need for society (e.g., to address the development of resistance to antibacterial drugs).”

B. Submission of Information on Negotiation Factors Related to Therapeutic Alternatives and Unmet Need (Section 1194(e)(2))

CMS’s approach and processes for collecting information on the negotiation factors related to therapeutic alternatives and unmet medical need should ensure that a robust, comprehensive set of information submitted by manufacturers– with any necessary supplemental material – will be accepted and considered by CMS.

The negotiation guidance references the Negotiation Data Elements ICR, which describes how CMS intends to collect data on the negotiation factors. We are concerned that CMS’s approach may be too limiting in practice and will not allow for a robust submission of information - including any supplementary material – by manufacturers. We will be providing more detailed comments on the ICR, but note Questions 40 through 43, which collect information on prescribing data, therapeutic impact and comparative effectiveness, comparative effectiveness in specific populations, and unmet medical needs. The data fields are limited to 1,000-3,000 words, which is insufficient in length. Further, the data fields do not seem to contemplate submission of complementary information, such as charts and tables. We strongly recommend that CMS reconsider its approach and permit manufacturers to submit any information they determine relevant to the negotiation process (including information not related to the negotiation factors enumerated in the statute). Further, CMS should be required to consider all such information, not just the negotiation factors in sections 1194(e)(1) and 1194(e)(2).

¹⁵⁴ <https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf>



C. Submission of Manufacturer-Specific Data (Section 1194(e)(1))

We understand that the IRA requires CMS to consider factors under both section 1194(e)(1) and section 1194(e)(2). **However, as noted above, we believe CMS should de-emphasize factors the manufacturer-specific data in section 1194(e)(1) and focus on the factors that matter most to patients – those that are focused on clinical value and unmet need. In addition, to address issues that we highlight below, we recommend that, in lieu of the proposed standardized definitions, CMS allow manufacturers to use reasonable assumptions (with accompanying justifications) regarding the information they submit on the manufacturer-specific data.**

There are important considerations that will make it difficult – if not impossible – for CMS to standardize the definitions for the manufacturer-specific factors. For example, regarding research and development costs, a key issue for CMS to consider is that companies, and investors, invest in research and development for “programs” in a specific disease area, not simply discrete drugs. A program can have many drugs or biologicals at different stages of development each with multiple indications, and all which would factor into the research and development costs for an FDA-approved or licensed therapy. This can include thousands and sometimes millions of compounds that could be screened early in the research and development process, with a success rate of less than 12%.¹⁵⁵

Further, it can be misleading to approximate “value” using research and development costs. Not all companies conduct research and development in the same manner. Some smaller companies might undertake single-therapeutic, high-risk approaches to developing a compound, while many others, often bigger companies, conduct research using the “programs,” as noted. These differences in the way research and development can be conducted could disadvantage companies in negotiation if manufacturer-specific data is too heavily relied upon for “value.”

Looking at research and development costs in the post-market setting can also be misleading because of ongoing costs that are difficult to quantify. For example, the FDA requires post-market safety monitoring, these costs can also be augmented if a manufacturer must utilize FDA-mandated risk evaluation and mitigation strategies (REMS), something to which not every manufacturer is subjected. Another example is costly post-market clinical trials that can take years.

We also are concerned with CMS’s proposed requirement to collect information that is not collected today – once example is net revenue “without patient assistance programs.” It is unclear why CMS would be collecting data in this manner and the underlying implication of patient assistance programs on price.

¹⁵⁵ Biopharmaceutical Research and Development: The Process Behind the Medicines, PhRMA. 2015. Accessed: 03/28/2023. http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf



In other areas, the definitions CMS proposes are unclear, which will make it difficult for manufacturers to comply with submission requirements. For example, regarding data on approved and pending patents, clarifications are required to better define the patents and pending patent applications that must be disclosed. More precision is required where CMS is asking for patents “relating” or “linked to” the selected drug, as it is unclear what CMS means – related or linked how? In this respect, we also note that “patent” and “patent application” are well-understood terms of art that don’t require further definition in the CMS guidance. For example, the CMS guidance definition of a “pending patent application” specifies any patent application “for which a patent number has not been issued.” This definition would plainly include applications that are not, in fact, pending because they have been abandoned. An “approved patent application” presumably means a patent application that has received a notice of allowance, meaning that it is still a pending patent application (and not a “patent”) that does not require a special definition. And a “patent” comes into existence not on the date a patent application is “approved,” but on the date a patent is issued, and the official patent grant is transmitted. We recommend deleting the special definitions of “pending patent application,” “approved patent application,” and “expired patent,” and to change the operative language as suggested in our proposed edits below.¹⁵⁶

Patents, Exclusivities, and Approvals

For the purposes of describing patents, exclusivities, and approvals to be collected for use in the Negotiation Program for the selected drug, as described in section 1194€(1) of the Act and section 50.1 of this memorandum, CMS intends to adopt the definitions described in this subsection.

- *CMS considers patents relevant to this data to include:*
 - *all patent applications pending in the USPTO, international patent applications filed under the Patent Cooperation Treaty that designate the United States, and all U.S. patents, that are owned by, licensed to, or controlled ~~pending and approved patent applications, including expired and non-expired approved patents, submitted, sponsored, licensed, and/or acquired by the Primary Manufacturer relating to the,~~ and that claim the selected drug, a constituent part of the selected drug, or an approved method of using the selected drug as of September 1, 2023;*
 - *U.S. patents ~~linked to~~ that claim the selected drug, a constituent part of the selected drug, or an approved method of using the selected drug where the Primary Manufacturer is not listed as the assignee/applicant but with respect to which the manufacturer has enforcement rights (for example, for a joint venture product); and any patent that is with respect to the selected drug included in a list published under*

¹⁵⁶ Note that the nomenclature of “Primary Manufacturer” is retained in the edits we suggest but we note our comments later in this section that raise concerns with the “Primary Manufacturer” and “Secondary Manufacturer” construct.



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section 351(k)(9) of the Public Health Service Act or section §505(j)(7) of the Federal Food, Drug, and Cosmetic Act, ~~patent applications, pending and approved~~, for which a claim of patent infringement could reasonably be, or has been, asserted against a person engaged in the unlicensed manufacture, use, or sale of the selected drug in any form.

More fundamentally, CMS states it will consider the length of available patents and exclusivities and, if such patents and exclusivities will last for a number of years, the Agency may consider reducing the preliminary price downward. BIO strongly opposes such an approach. Rather, remaining patents and exclusivities should only be used to justify an *increase* in the preliminary price.

Regarding data on prior federal financial support in discovery and development, important contextual information should be considered by CMS. The biopharmaceutical industry's role in the U.S. research ecosystem is to undertake the clinical research and development required to advance basic science research by entities such as the National Institutes of Health (NIH) into safe and effective treatments available to patients. In 2018, the biopharmaceutical industry invested \$102 billion in R&D, most of which was focused on clinical research. Meanwhile, the entire NIH budget in 2018 was \$35.4 billion, only 8% of which was focused directly on clinical research.

Of note, of the 23,230 NIH grants in the year 2000 that were linked by NIH supported patents to 41 investigational drugs, only 18 had gained FDA approval by 2020. In fact, total private investment for these 18 approved medicines exceeded NIH funding by substantial orders of magnitude: \$44.2 billion in private investment compared to \$670 million in NIH. These findings are consistent with scholarship describing the complementary roles of public and private R&D funding, and the significant long-term investments shouldered by industry with no guarantee of approval. In fact, just 7.9% of medicines in clinical development are ultimately approved by the FDA.¹⁵⁷

We also note our concern with the proposal to hold a Primary Manufacturer responsible for submitting applicable information concerning a Secondary Manufacturer. A Primary Manufacturer has no inherent legal authority to compel a Secondary Manufacturer to act or not act, including to share such information. It would be fundamentally unfair and legally problematic for CMS to threaten a Primary Manufacturer with significant civil monetary penalties (CMPs) for failure to do the impossible. We note that this same concern pervades the Initial Guidance, given the numerous contexts in which CMS proposes to hold a Primary Manufacturer responsible for the action or inaction of a Secondary Manufacturer.

¹⁵⁷ Clinical Development Success Rates and Contributing Factors 2011-2020. Available at [bio.org](https://www.bio.org).



V. MFP Ceiling

A. Background

The calculation of the MFP ceiling, which represents the maximum possible MFP, is the lowest of three amounts:

- (1) the “applicable percent” of the Average Non-FAMP for 2021 (or, if there is such Non-FAMP, the Average Non-FAMP for the first full year following market entry), as increased by a Consumer Price Index for All Urban Consumers (CPI-U) factor;¹⁵⁸
- (2) the “applicable percent” of the Average Non-FAMP for the year before the year of the selected drug publication date (except for IPAY 2026);¹⁵⁹ or
- (3) (a) for a Part D drug, the sum of each “plan specific enrollment weighted amount” for each prescription drug plan (PDP) or Medicare Advantage prescription drug (MA-PD) plan;¹⁶⁰ or
(b) for a Part B drug, the Part B payment amount for the year before the year of the selected drug publication date.¹⁶¹

The “applicable percent” is 75 percent for “short-monopoly drugs,”¹⁶² 65 percent for “extended-monopoly drugs,”¹⁶³ and forty percent for “long-monopoly drugs.”¹⁶⁴

B. Average Non-FAMP

BIO recommends that, in defining Average Non-FAMP, CMS abandon its proposal to create a new price point calculated based on the four quarters of a calendar year, and instead simply adopt the existing annual Non-FAMP, calculated based on the four quarters of a federal fiscal year, under the Veterans Health Care Act of 1992 (VHCA).

As set forth above, Average Non-FAMP is calculated as part of determining the MFP ceiling.¹⁶⁵ Average Non-FAMP is a statutory term of art meaning “the average of the non-Federal average manufacturer

¹⁵⁸ SSA § 1194(c)(1)(A), (C). The CPI-U adjustment applies from September 2021 (or December of the first full year following market entry) to September of the year before the year of the selected drug publication date.

¹⁵⁹ *Id.*

¹⁶⁰ *Id.* § 1194(c)(1)A, (B)(i), (2).

¹⁶¹ *Id.* § 1194(c)(1)(A), (B)(ii).

¹⁶² *Id.* § 1194(c)(3)(A) (defining “short monopoly drug” as a selected drug that is not an “extended-monopoly drug” or “long-monopoly drug”).

¹⁶³ *Id.* § 1194(c)(3)(B); *see also id.* § 1194(c)(4) (defining “extended monopoly-drug”).

¹⁶⁴ *Id.* § 1194(c)(3)(C); *see also id.* § 1194(c)(5) (defining “long-monopoly drug”).

¹⁶⁵ *Id.* § 1194(c)(1)(A), (C).



price (as defined in section 8126(h)(5) of title 38, United States Code) for the 4 calendar quarters of the year involved.”¹⁶⁶

The statute does not specify which four quarters are “the 4 calendar quarters of the year involved but notably cross-references 38 U.S.C. § 8126(h)(5), i.e., the VHCA. As such, the statute effectively instructs CMS to calculate Average Non-FAMP by reference to how annual Non-FAMP is calculated under the VHCA.

The VHCA requires manufacturers to calculate and report quarterly Non-FAMPs and an annual Non-FAMP—but does not require manufacturers to calculate and report an “average” Non-FAMP based on the four quarters of a calendar year. Rather, the annual Non-FAMP is calculated based on the four quarters of a federal fiscal year—which runs from October 1 through September 30.¹⁶⁷

As such, the annual Non-FAMP is a stand-alone weighted average calculation based on data from the fourth quarter of a calendar year through the third quarter of the subsequent calendar year (i.e., the four quarters of a federal fiscal year).¹⁶⁸ The most coherent policy would be for CMS to adopt the same approach to calculating Average Non-FAMP for a year under the Negotiation Program. Given that the statute expressly cross-references the VHCA in the course of defining Average Non-FAMP, there is every reason to think that Congress wanted CMS to maximize alignment as between Average Non-FAMP and the annual Non-FAMP under the VHCA, rather than creating an entirely new price point.

In the Initial Guidance, however, CMS does not propose to borrow the established VHCA framework. Rather, CMS proposes to calculate Average Non-FAMP by reference to the four quarter of a calendar year.¹⁶⁹ This approach is inefficient and unnecessarily burdensome for both CMS and manufacturers. Under the proposal, the Agency will be obligated to develop, implement, and oversee a completely new process to facilitate collection of new pricing data, as the Agency cannot benefit from the efficiencies of the well-established process that VA has already put into place—because the VHCA approach is, as noted above, tied to a federal fiscal year, rather than a calendar year. By contrast, if the Agency instead were to borrow the existing VHCA framework, Average Non-FAMP would be equated with a price point that already exists, and all stakeholders would benefit from the resulting efficiencies.

¹⁶⁶ *Id.* § 1194(c)(6).

¹⁶⁷ For example, the data used to calculate the annual Non-FAMP for 2021 cover the period from October 1, 2020, through September 30, 2021.

¹⁶⁸ The annual and quarter 3 Non-FAMPs submitted to the Department of Veterans Affairs (VA) are used to calculate the Federal Ceiling Price (FCP), which caps pricing under VA Federal Supply Schedule contracts. Manufacturers are required to submit quarters 1, 3, and 4 Non-FAMPs, too, but these price points have no impact on the price paid by the federal government. While the data used to calculate these quarterly Non-FAMPs are incorporated into the four quarters of data used to calculate the annual Non-FAMP, these quarterly Non-FAMPs themselves are not used to calculate the annual Non-FAMP.

¹⁶⁹ Initial Guidance at 42–44.



If CMS does not reverse course, BIO agrees that CMS’s framework should be based on a weighted average.¹⁷⁰

A weighted average is consistent with the VHCA framework expressly cross-referenced in the statutory definition of Average Non-FAMP. As such, a weighted average better aligns to Congress’s intent.

More importantly, use of a weighted average will objectively enhance accuracy because it will account for differences in volume across quarters and therefore create the most accurate picture of average wholesaler pricing. Such enhanced accuracy is why Congress has consistently required the use of weighted averages across the various federal pricing programs associated with federal health care programs: VHCA (Non-FAMP), Medicaid (AMP), and Medicare (ASP) all use weighted averages, not simple averages.

Congress has consistently required the use of weighted averages because simple averages are less accurate. Simple averages result in over-valuation of sales in quarters with lower sales volumes, and under-valuation of sales in quarters with higher sales volumes. As such, it is critically important that CMS use a weighted average to ensure more accurate calculations of Average Non-FAMP, and we concur with CMS’s proposal to do so.

The Agency should establish an exceptions process to account for restatements and anomalies.

An exceptions process is vital. There will inevitably be situations where Average Non-FAMP will need to be restated in light of data errors or other issues identified after the fact or where an unusual circumstance will result in an anomalous Average Non-FAMP.

- **Non-FAMP restatements.** CMS must consider how it will address situations in which a Non-FAMP that is used for an MFP calculation is restated by the manufacturer and approved by VA. VA has long recognized the need for manufacturers to be able to restate a Non-FAMP where the reported Non-FAMP is determined to be inaccurate (e.g., sales data flaws, data system problems). The VA experience has demonstrated that restatements are not uncommon, with adjustments of contract pricing facilitated based on restated Non-FAMPs and FCPs. The Agency must expressly account for the need for such restatements—but the Initial Guidance does not do so.

¹⁷⁰ *Id.* at 43.



- **Non-FAMP anomalies.** The VA's experience reveals a variety of circumstances where an anomalous Non-FAMP can arise due to a misalignment of sales dollars and units. This can occur due to lagged sales, market shortages, or various other factors. VA has developed various exceptions and workarounds for calculating FCPs when there are Non-FAMP anomalies. It is vital that CMS develop its own processes for addressing anomalous Average Non-FAMPs. Any approach adopted by CMS needs to be flexible to account for the wide range of circumstances that can result in an anomalous Average Non-FAMP.¹⁷¹ But the Initial Guidance is silent on any such flexibilities.

BIO encourages CMS to adopt an exceptions process to account for Average Non-FAMP restatements and anomalies. In doing so, CMS should clarify how such process affects the MFP ceiling and, ultimately, the MFP.

C. Extended- and long-monopoly drugs

CMS should clarify whether the time period for determining whether a selected drug is an extended- or long-monopoly drug runs to the start of the applicable IPAY, or to the applicable selected drug publication date.

As set forth above, there are three options for setting the MFP ceiling. Two of these options look to the “applicable percent” of the applicable Average Non-FAMP.¹⁷² By statute, the “applicable percent” varies based on whether the drug is a short-, extended-, or long-monopoly drug.¹⁷³

With limited exceptions, extended monopoly drugs are, “with respect to an initial price applicability year, selected drug[s] for which at least 12 years, but fewer than 16 years, have elapsed since the date of approval . . . or . . . licensure,”¹⁷⁴ and long-monopoly drug are, “with respect to an initial price applicability year, selected drug[s] for which at least 16 years have elapsed since the date of approval . . . or licensure.”¹⁷⁵ Short-monopoly drugs are all other selected drugs.¹⁷⁶

Notably, the statute is silent as to the date to which the twelve- or sixteen-period that defines an extended- or long-monopoly drug runs. In the Initial Guidance, CMS takes inconsistent positions. On the one hand, CMS states that, for IPAY 2026, a delay request may be submitted where a reference

¹⁷¹ For example, in certain cases, it may be prudent for CMS to account for an Average Non-FAMP anomaly by looking to the prior year's figures; in other cases (e.g., a new product), this may not be possible.

¹⁷² SSA § 1194(c)(1).

¹⁷³ *Id.* § 1194(c)(3).

¹⁷⁴ *Id.* § 1194(c)(4)(A).

¹⁷⁵ *Id.* § 1194(c)(5)(A).

¹⁷⁶ *Id.* § 1194(c)(3)(A).



biologic will have been “licensed for between 12 and 16 years prior to the start of the initial price applicability year on January 1, 2026.”¹⁷⁷ On the other hand, in “Figure 2: Monopoly Types and Applicable Percentage for Initial Price Applicability Year 2026,” CMS conveys that, for IPAY 2026, it will count the 16-year period that defines a long-monopoly drug to September 1, 2023, i.e., the selected drug publication date for IPAY 2026.¹⁷⁸ In other words, CMS is inconsistent as to whether the twelve- or sixteen-year period that defines an extended- or long-monopoly drug runs to the start of the applicable IPAY, or to the applicable selected drug publication date.

BIO asks CMS to clarify its intended interpretation in light of the conflicting language in the Initial Guidance.

D. MFP ceiling for Part D drugs

BIO disagrees with CMS’s intended approach for calculating the MFP ceiling option specific to Part D drugs. CMS must calculate the MFP ceiling under such option exclusive of manufacturer price concessions unless they are passed through at the point of sale, consistent with CMS’s long-standing policy governing the Part D negotiated price.

As set forth above, one of the three options for determining the MFP ceiling with respect to a Part D drug is the sum of each “plan specific enrollment weighted amount” for each PDP or MA-PD plan.¹⁷⁹ Congress specified that the “plan specific enrollment weighted amount” is determined by reference to the Part D negotiated price.¹⁸⁰ As such, Congress made clear that the “plan specified enrollment weighted amount” is to be determined by reference to CMS’s policies governing the Part D negotiated price.

This is not what CMS proposes. In the Part D context, CMS has long defined the Part D negotiated price to be “inclusive of all price concessions from network pharmacies, except those contingent price concessions that cannot reasonably be determined at the point-of-sale”—but not to require inclusion of price concessions from manufacturers.¹⁸¹ Rather, PDPs and MA-PDs may choose to include manufacturer price concessions in the Part D negotiated price to the extent that they are passed through at the point of sale: “Part D sponsors are allowed, but generally not required, to apply rebates

¹⁷⁷ Initial Guidance at 17 (emphasis added).

¹⁷⁸ See Initial Guidance at 45.

¹⁷⁹ SSA § 1194(c)(1) (A), (B)(i).

¹⁸⁰ *Id.* § 1194(c)(2).

¹⁸¹ 42 C.F.R. § 423.100 (emphasis added). CMS has issued a rule that will revise the Part D negotiated price definition effective January 1, 2024. But such revision does not alter the fact that the Part D negotiated price does not require inclusion of manufacturer price. See 87 Fed. Reg. 27,704, 27,899 (May 9, 2022).



and other price concessions at the point of sale to lower the price upon which beneficiary cost-sharing is calculated.”¹⁸²

CMS’s Initial Guidance ignores this long-standing policy defining the Part D negotiated price. For purposes of calculating the MFP ceiling under the option specific Part D drugs, CMS instead proposes to use Direct and Indirect Remuneration (DIR) data—rather than solely PDE data—to calculate the “plan specific enrollment weighted amount.”¹⁸³ Notably, unlike PDE data, DIR data reflect all price concessions, including those received from manufacturers that are not passed through at the point of sale.¹⁸⁴

CMS’s proposed approach is contrary to statute, which makes clear that the MFP ceiling option must be determined by reference to the Part D negotiated price. By choosing expressly to define the MFP ceiling option by reference to the Part D negotiated price, Congress required such option to be calculated in accordance with policy governing the calculation of the Part D negotiated price. Any contrary approach would render meaningless Congress’s express choice to use the Part D negotiated price as the statutory reference point.

In addition to being inconsistent with statutory text and Congressional intent, CMS’s proposal also would create significant unnecessary complexities. It would be more burdensome for the Agency to determine the MFP ceiling for Part D drugs if the Agency were to apply a standard that is inconsistent with the Part D standard. In addition, it would impose a new and unfamiliar approach on pharmacies, plans, pharmacy benefit managers (PBMs), manufacturers, and other stakeholders, and would thereby increase the risk of confusion or error that could result in an erroneous MFP.

BIO urges CMS to abandon this proposal and instead align the Part D drug-specific MFP ceiling option with CMS’s long-standing policy defining the Part D negotiated price, consistent with the requirements of the statute.

VI. Providing Access to the MFP

A. Background

Under the Negotiation Program, the manufacturer of a selected drug must provide access to the MFP to:

¹⁸² 87 Fed. Reg. at 27,835 (the Part D negotiated price is “the price paid to the network pharmacy or other network dispensing provider for a covered Part D drug dispensed to a plan enrollee that is reported to CMS at the point of sale by the Part D sponsor”).

¹⁸³ Initial Guidance at 40.

¹⁸⁴ CMS, Medicare Part D – Direct and Indirect Remuneration (DIR) (Jan. 19, 2017).



- With respect to a Part B drug, “hospitals, physicians, and other providers of services and suppliers with respect to [individuals who are enrolled under Part B, including individuals who are enrolled in an Medicare Advantage (MA) plan, if payment may be made under Part B for the drug, and who are furnished the drug];”¹⁸⁵ and
- With respect to a Part D drug, “[individuals who are enrolled in a PDP or MA–PD plan if the drug is covered under such plan, and who are dispensed the drug,] at the pharmacy, mail order service, or other dispenser at the point-of-sale of such drug (and . . . to the pharmacy, mail order service, or other dispenser, with respect to such . . . individuals who are dispensed such drugs).”¹⁸⁶

MFP-340B duplicate discounts are prohibited: The manufacturer is required to provide access to either the MFP or the 340B price, whichever is lower.¹⁸⁷

B. MFP rebate model

BIO commends CMS for proposing that access to the MFP may be provided through an MFP rebate model and urges the Agency to clarify that the proposed fourteen-day period during which an MFP rebate must be paid runs from the date on which the manufacturer has validated eligibility for the rebate.

CMS proposes that a manufacturer may provide access to the MFP by either (1) ensuring that the price paid when acquiring the drug is no greater than the MFP or (2) providing retrospective reimbursement for the difference between the acquisition cost and the MFP.¹⁸⁸ BIO commends this approach.

Generally speaking, the manufacturer of a selected drug must provide access to the MFP to providers and pharmacies with respect to Part B, MA, and Part D beneficiaries.¹⁸⁹ It follows that the manufacturer has no obligation to provide access to the MFP to providers and pharmacies on units that will be furnished or dispensed to individuals who are not Part B, MA, or Part D beneficiaries (MFP-ineligible individuals).

An MFP rebate model is vital because it enables prospective safeguarding against diversion of MFP units to MFP-ineligible individuals. This is essential because the statute does not provide any retrospective

¹⁸⁵ SSA § 1193(a)(3)(B); *see also id.* § 1191(c)(2)(B).

¹⁸⁶ *Id.* § 1193(a)(3)(A); *see also id.* § 1191(c)(2)(A).

¹⁸⁷ *Id.* § 1193(d).

¹⁸⁸ Initial Guidance at 40.

¹⁸⁹ *Id.* § 1193(a)(3); *see also id.* § 1191(c)(2).



mechanism for doing so. For example, the statute does not provide any post-hoc audit right to either the manufacturer or CMS to validate that providers and pharmacies have appropriately furnished or dispensed MFP units. Nor is there any post-hoc dispute resolution mechanism that enables the manufacturer to contest and recover the MFP discount on units that were improperly furnished or dispensed. Likewise, the statute does not grant CMS authority to impose CMPs or other sanctions, such as termination of access to the MFP, on providers and pharmacies that engage in diversion. Under these circumstances, CMS must establish a means to prospectively prevent diversion of MFP units. Authorizing an MFP rebate model is the most logical and practical means of doing so. It provides a mechanism through which the manufacturer can confirm that a unit was in fact furnished or dispensed to an MFP-eligible individual before providing access to the MFP.¹⁹⁰

Absent an MFP rebate model, there would be no way to mitigate against unlimited diversion of MFP units. And this is not a merely theoretical concern. In contrast to the Negotiation Program, the 340B Program, which is generally administered via upfront discounts, features a statutory audit right, a statutory dispute resolution mechanism, and agency authority to impose sanctions, including termination of access to the 340B price.¹⁹¹ Yet even this constellation of statutory safeguards against diversion has proven deeply inadequate to prevent diversion of 340B units.¹⁹² In the face of this well-documented real world experience, it would be patently unreasonable if CMS were to require upfront MFP discounts with no such safeguards. Indeed, doing so would be impermissible, as it would be tantamount to nullifying the express limitation on the obligation to provide access to the MFP only with respect to MFP-eligible individuals.¹⁹³

A rebate model is also the most administratively straightforward means of providing access to the MFP. The rebate model is commonplace in the commercial sector and under Part D, such that an MFP rebate model can be implemented as seamlessly and efficiently as possible and in a manner well familiar to all

¹⁹⁰ As a manufacturer can confirm when it submits its “process for making the MFP available,” Initial Guidance at 32, the minimum necessary Medicare claims data will be used to validate eligibility for the MFP, and reasonable time frames for submission of a request for, validation of eligibility for, and payment of an MFP rebate will be established. Additionally, providers and pharmacies will know at the time that a unit of a drug is furnished or dispensed that the drug is a selected drug and its associated MFP-based cost-sharing. As such, an MFP rebate model will not interfere with timely access by MFP-eligible individuals to MFP-based cost-sharing.

¹⁹¹ PHSA § 340B(a)(5)(C), (d)(2)(B)(v), (3).

¹⁹² See, e.g., Examining HRSA’s Oversight of the 340B Drug Pricing Program: Hearings Before the Subcomm. on Oversight & Investigations of the H. Comm. on Energy & Commerce, 115th Cong. 2–3 (2017) (noting limited oversight against diversion and that between 63 and 82 percent of audited 340B covered entities have been found to be noncompliant with at least one program requirement) (statement of Rep. Tim Murphy), available at <https://www.congress.gov/115/chrg/CHRG-115hhrg26929/CHRG-115hhrg26929.pdf>; T. Okon, *Hospitals and for-profit PBMs are diverting billions in 340B savings from patients in need*, Stat News, <https://www.statnews.com/2022/07/07/for-profit-pbms-diverting-billions-340b-savings/> (June 7, 2022); see also PHSA § 340B(a)(5)(B).

¹⁹³ *Whitman v. Am. Trucking Ass’n, Inc.*, 531 U.S. 457, 484 (2001) (an agency may not implement a statute in a manner that “completely nullifies” an otherwise applicable provision).



stakeholders. And CMS has clear legal authority to permit an MFP rebate model, as the statute does not specify how the manufacturer of a selected drug must provide access to the MFP, and, what is more, the statute grants CMS broad discretion to “establish[] . . . procedures to carry out the provisions of [the Negotiation Program], as applicable, with respect to [MFP-eligible individuals].”¹⁹⁴

To ensure smooth integration of the rebate model, and because only pharmacies know the actual acquisition cost (AAC), BIO recommends CMS define the MFP discount using a publicly reported metric, such as wholesale acquisition cost (WAC).

BIO is concerned with the metric CMS is proposing to use when defining the MFP discount, the AAC. CMS proposes that manufacturers that provide access to the MFP using a rebate model will need to provide the pharmacy a discount equal to the difference between the pharmacy’s acquisition cost, or the AAC, and the MFP. Among others, there are concerns with accessibility of the pharmacy’s AAC as it is currently not known to entities beyond the pharmacy. BIO recommends CMS define the MFP discount using a publicly reported metric, such as wholesale acquisition cost (WAC).

To facilitate a functional rebate model, BIO urges CMS to clarify that the proposed fourteen-day period during which an MFP rebate must be paid runs from the date on which the manufacturer has validated eligibility for the rebate.

CMS proposes that the manufacturers provide retrospective reimbursement within fourteen days. But the Initial Guidance is silent on when the clock begins to run. CMS should clarify that the clock begins to run on the date on which the manufacturer has validated eligibility for the rebate, in accordance with commercial sector conventions. In fact, this is the only rational starting point.

If CMS were instead to suggest that the clock begins to run on the date on which the rebate is requested, there would be insufficient time for the manufacturer to confirm that the unit was in fact furnished or dispensed to an MFP-eligible individual before providing access to the MFP—and, more fundamentally, no incentive for a provider or pharmacy to provide any validating Medicare claims data (including the 340B and non-340B claims modifiers discussed in section VI.C). This would render the rebate model completely nugatory, as such data are essential to the rebate model. Alternatively, we believe CMS should require providers to furnish claims level data such that it is required to process an individual claim, including the 340B or non-340B claims modifier as necessary. As CMS notes in its communication to states entitled, “Best Practices for Avoiding 340B Duplicate Discounts in Medicaid,” manufacturer access to claims level data is likely needed for invoice validation.¹⁹⁵ The rebate model is

¹⁹⁴ SSA § 1196(a)(3).

¹⁹⁵ Best Practices for Avoiding 340B Duplicate Discounts in Medicaid, CMS, January 8, 2020. https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/cib010820_1.pdf.



useful only to the extent that it provides a meaningful opportunity to prospectively safeguard against statutorily prohibited diversion of MFP units to MFP-ineligible individuals. As such, the rebate payment clock must begin ticking only after the manufacturer has verified the propriety of the rebate. Any contrary approach would be both plainly irrational and run directly contrary to the clear intent of Congress, which declined to impose any obligation on the manufacturer to provide access to the MFP with respect to an MFP-ineligible individual.¹⁹⁶

To promote efficiency and program integrity and to minimize the burden on interested parties, CMS should adopt a third-party administrator or clearinghouse rebate model.

Finally, BIO strongly urges CMS to utilize a CMS-established third-party administrator (TPA) for the rebate model. By utilizing a TPA, CMS can ensure prompt payment while promoting efficiency and program integrity and minimizing obligations on stakeholders. The CMS-established TPA would also need to serve as a Medicare claims data clearinghouse. To enable manufacturers that choose the rebate option to validate the propriety of MFP rebate invoices, CMS should require all necessary claims level data be shared with the clearinghouse such that it is required to process an individual claim, including the 340B or non-340B claims modifier. The TPA clearinghouse would also be an effective way to ensure non-duplication between the MFP and the 340B program.

C. MFP-340B Duplicate Discounts

To prevent MFP-340B duplicate discounts, BIO urges CMS to condition payment of a claim for reimbursement for a unit of a selected drug on the accurate use of *either* a 340B or a non-340B claims modifier, across Part B, MA, and Part D.

As set forth above, the statute prohibits MFP-340B duplicate discounts.¹⁹⁷ To make this statutory prohibition meaningful, CMS must establish a mechanism that meaningfully allows manufacturers to avoid MFP-340B duplicate discounts across Part B, MA, and Part D.

With respect to Part B, CMS has already taken steps toward establishing such a mechanism. Effective January 1, 2024, all 340B covered entities that submit a Part B claims must use a 340B claims

¹⁹⁶ In the alternative to requiring payment of an MFP rebate within fourteen days of the date on which the manufacturer has validated eligibility for the rebate, CMS could requirement payment of an MFP rebate either (1) within thirty days of the date on which the provider or pharmacy submits all necessary validating Medicare claims data, to be tolled during the pendency of a reasonable dispute resolution process or (2) within 45 days of the date on which the provider or pharmacy submits all necessary validating Medicare claims data. Notably, if the clock were to begin to run before the submission of such data, it would render the rebate model pointless, as the entire point of the model is to enable the manufacturer to validate eligibility for the rebate.

¹⁹⁷ *Id.* § 1193(d) (the manufacturer is required only to offer the lower of the MFP and the 340B price).



modifiers.¹⁹⁸ With respect to Part D, CMS has similarly proposed to require a 340B identifier in prescription drug event (PDE) file, acknowledging that “requiring that a 340B indicator be included on the [PDE] record is the most reliable way to identify drugs that are subject to a 340B discount that were dispensed under Medicare part D,” for purposes of excluding 340B units from the Part D inflation rebate calculation.¹⁹⁹

BIO appreciates these steps, but CMS must take additional steps to make the prohibition of MFP-340B duplicate discounts meaningful. As a start, CMS must require the use of either a 340B modifier or a non-340B modifier, and condition payment of a claim on the accurate use of the applicable modifier. And CMS must implement the same constellation of essential safeguards with respect to MA units. All such safeguards are necessary to ensure that 340B covered entities are properly incentivized to accurately identify 340B units. And such safeguards must be paired with an MFP rebate model to prospectively guard against MFP-340B duplicate discounts, given the absence of a statutory mechanism for retrospectively doing so.²⁰⁰ Any other safeguards necessary to protect against MFP-340B duplicate discounts should be adopted as well.

The need for such protections is readily apparent in light of the long history of improper duplicate discounts in analogous contexts: There continues to be widespread 340B covered entity non-compliance issues with respect to the MDRP-340B duplicate discount prohibition.²⁰¹ The same risk is present with respect to MFP-340B duplicate discount, and CMS must establish a mechanism to guard against them, as the prohibition against MFP-340B duplicate discounts is meaningful only if CMS does so. “An administrative agency cannot abdicate its responsibility to implement statutory standards under the guise of determining that inaction is the best method of implementation.”²⁰²

D. Providing access to the MFP to Part D beneficiaries at the point of sale

BIO concurs with CMS that a manufacturer is not required to provide access to the MFP to Part D beneficiaries at the point of sale *directly*.²⁰³

¹⁹⁸ CMS, Part B Inflation Rebate Guidance: Use of the 340B Modifiers 1 (Dec. 20, 2022), *available at* <https://www.cms.gov/files/document/part-b-inflation-rebate-guidance340b-modifierfinal.pdf>.

¹⁹⁹ CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum 18 (Feb. 9, 2023), *available at* <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>.

²⁰⁰ See § VI.B *supra*.

²⁰¹ See, e.g., Government Accountability Office, *Drug Discount Program: Federal Oversight of Compliance at 340B Contract Pharmacies Needs Improvement* (2018), *available at* <https://www.gao.gov/assets/gao-18-480.pdf>; see also PHSA § 340B(a)(5)(A).

²⁰² *United States v. Markgraf*, 736 F.2d 1179, 1183 (7th Cir. 1984).

²⁰³ Initial Guidance at 31.



In the Initial Guidance, CMS correctly recognizes that access to the MFP must be provided to Part D beneficiaries at the point of sale through PDPs or MA-PDPs, as opposed to the manufacturer (as a literal reading of the statute might suggest).²⁰⁴ This is because it is impossible for a manufacturers to provide access to the MFP to Part D beneficiaries at the point of sale directly because they are not a party to the transaction at the point of sale. Rather, the point-of-sale transaction is among the Part D beneficiary, the pharmacy, and the plan or its PBM. Not only are manufacturers not a party to the transaction at the point of sale, but they are also typically not even in privity of contract with the point-of-sale pharmacy (and may also not even be in privity of contract with the plan or its PBM). As such, the only rational way to operationalize the statutory directive is for CMS to establish a pathway by which the MFP is passed through to Part D beneficiaries by those that are parties to the point-of-sale transaction. Therefore, BIO concurs with CMS’s clarification that access to the MFP by Part D beneficiaries at the point of sale will be effectuated through plans, not manufacturers.

E. Application of the MFP Across Dosage Forms and Strengths

We request that CMS simplify its proposed approach and address concerns with its proposed methodology.

In section 60, CMS proposes a complicated set of comparisons for purposes of creating a single proposed MFP for each drug for negotiation purposes. BIO understands the agency’s application of the statutory directive to create a “maximum fair price across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug.” However, the agency’s decision, discussed above to treat products that are the subject of discrete NDAs as the same drug because they have the same active moiety, unnecessarily compounds the complexity of this effort. In many cases, products requiring significantly different routes of administration treat different conditions or have different clinical profiles—which results in a requirement for discrete NDAs to establish that the use of these therapies is safe and effective. In addition, drugs with different routes of administration may have substantially different manufacturing costs.

Thus, while BIO understands what the agency was attempting to accomplish in the system it has proposed for resolving the calculation of MFP across all dosage forms and strengths, the complexity of the system is compounded by CMS’ desire to include, in a single calculation, products with multiple routes of administration that will often be approved under multiple NDAs as separate drugs. The calculation also relies upon standardized concepts of 30-day equivalent supply, which may or may not have a true equivalence, especially for any products with some formulations dosed once via injection to

²⁰⁴ SSA § 1193(a)(3).



last a longer period of time which may not be standardized across all clinical practice—and may differ markedly from oral formulations for the same chemical. The complicated equation CMS has established may not be able to adequately resolve these differences when calculating a standardized MFP across all forms and strengths of particular chemical compounds—and it need not do so for products approved under separate NDAs that should be treated as different drugs for purposes of MFP calculations.

BIO urges CMS to simplify MFP calculations by following the statutory language of the IRA and attempt to create a single MFP only for dosage forms of each drug that are identified by reference to the same NDA or BLA. Products that are separately approved should be treated as separate drugs. This will resolve much of the unnecessary complexity in the agency’s proposed calculations described in section 60.

In addition, BIO is concerned that the last step of the 10-step process CMS has outlined will create an additional round of price cuts on dosage forms and strengths which cost more than other dosage forms and strengths for the same product for purposes of these calculations. By selecting a single ceiling price for the MFP and then comparing it differentially to the NDC9 level ceiling prices for the different dosage form and strengths of products, CMS is effectively undermining its own “single” MFP ceiling. Products which cost more at the NDC9 level than the dosage form and strength level calculated in section 60.2.2 and 60.2.3 would be subjected to two rounds of cuts, one during the process outlined in section 60.5 and again during the negotiation process itself. This undermines the creation of a “single” MFP since the different dosage forms and strengths are not equally subjected to the two rounds of cuts. This could potentially penalize more expensive dosage forms and strengths and undermine the ability of manufacturers to continue to provide these products. Moreover, the differential impact of the CMS methodology across dosage forms and strengths could also result in inequitable patient cost sharing.

In sum, BIO urges CMS to consider ways to simplify its methodology for applying the MFP across different dosage forms and strengths to avoid these distortions. As noted, some of these issues could be mitigated if CMS treats products which are separately approved as separate drugs. In addition, BIO believes that the agency has the authority to apply the MFP using more simplified units of measure than the 30-day equivalent methodology CMS has proposed.

F. The Date on Which a Generic or Biosimilar Is Marketed and the Date on Which CMS Determines That a Generic or Biosimilar Has Been Marketed

It is imperative that CMS abandon its bona fide marketing standard. This standard for determining the date of marketing of a generic or biosimilar is incompatible with the statute and contrary to sound public policy. CMS should instead adopt a standard that consistently designates the MDRP “market



date” as both the date on which a generic or biosimilar is marketed *and* the date on which CMS determines that a generic or biosimilar has been marketed.

The statute anchors multiple important provisions to either (1) the date on which a generic or biosimilar is marketed or (2) the date on which CMS determines that a generic or biosimilar is marketed.

With respect to the former date, a drug or biologic may be selected for negotiation only if, by the selected drug publication date, it is a qualifying single source drug—which excludes a drug or biologic with respect to which a generic or biosimilar is marketed.²⁰⁵ In addition, a biologic subject to a delay in selection for negotiation is rendered ineligible for selection for negotiation if a biosimilar is marketed by the date that is two years what otherwise would have been the selected drug publication date.²⁰⁶ And a biologic may not be subject to such a delay if more than one year has passed since the biosimilar was licensed and the biosimilar is not marketed.²⁰⁷

With respect to the latter date, most notably, a selected drug ceases to be subject to the MFP at the start of the year that is “at least 9 months after the date on which [CMS] determines that at least one generic or biosimilar has been marketed.”²⁰⁸ In addition, a drug or biologic ceases to be subject to negotiation if, by the end of the negotiation period, CMS determines that a generic or biosimilar has been marketed;²⁰⁹ and a non-compliant manufacturer of a selected drug subject to an ongoing excise tax ceases to be subject to such tax on the date on which CMS determines that a generic or biosimilar has been marketed.²¹⁰

In either case, the determination of the date of marketing of a generic or biosimilar is of enormous consequence throughout the program. CMS has stated its intent to use an ill-defined and complicated process to make what is in fact an entirely straightforward determination. CMS intends to review PDE data to determine whether a generic or biosimilar is marketed under a “bona fide marketing” standard that reflects CMS’s subjective assessment of whether the degree of utilization of the generic or biosimilar represents “robust and meaningful competition.”²¹¹

²⁰⁵ *Id.* § 1192(e)(1)(A)(iii); (B)(iii). The statute refers to a generic or biosimilar that is both approved or licensed and marketed. We focus only on the latter because the date of marketing should never fall before the date of approval or licensure.

²⁰⁶ *Id.* § 1192(f).

²⁰⁷ *Id.* § 1192(f)(2)(D)(iii).

²⁰⁸ *Id.* § 1192(c)(1) (emphasis added).

²⁰⁹ *Id.* § 1192(c)(2).

²¹⁰ Internal Revenue Code (IRC) § 5000D(b)(1)(B).

²¹¹ Initial Guidance at 67. BIO notes that, in some cases, the Initial Guidance does not specify whether the Agency intends to use the bona fide marketing standard to determine the date of marketing. In particular, it is unclear whether CMS intends to use such standard with respect to provisions regarding delay in the selection of a biologic for negotiation. If CMS intends to use an alternative standard with respect to such provisions, it should clearly articulate such alternative and subject it to public comment.



CMS’s approach is deeply problematic for myriad reasons. Foremost is that the bona fide marketing standard is contrary to the plain language of the statute: CMS’s standard is not rationally related to the actual date of marketing. As a definitional matter, marketing is “[t]he act[] . . . of bringing or sending a product or commodity to market.”²¹² As such, once the “action of buying or selling” has occurred, a product has necessarily been “marketed.”²¹³

CMS itself has long recognized that the date on which a product is “marketed” is an objective point-in-time determination of the date on which it is made available for sale in the commercial marketplace—including in the course of implementing other provisions of the IRA as well as under the Part D program which will source the data on which CMS intends to rely in effectuating its bona fide marketing standard. Mere months ago, CMS proposed to determine when a product is “marketed” for purposes of the IRA’s Part D inflation rebates by reference to the “market date” that the manufacturer must report under MDRP.²¹⁴ In turn, under MDRP, CMS has long defined the “market date” of a product by reference to the date on which the product entered commercial distribution, consistent with the plain language definition of “marketed.”²¹⁵ And, under the Part D program, which will source the PDE data on which CMS intends to rely in effectuating its bona fide marketing standard, CMS has recognized that the date on which a product is “release[d] onto the market” triggers certain coverage-related obligations²¹⁶—which by necessary implication means that CMS will have already recognized that a product has been released onto market by the time such coverage-related obligations yield PDE data showing utilization of the product.

²¹² Oxford English Dictionary, Definition of Marketing, <https://www.oed.com/view/Entry/114186?rskey=36dfg4&result=2&isAdvanced=false#eid> (last visited Mar. 19, 2023).

²¹³ *Id.*

²¹⁴ CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1860D-14B of SSA, and Solicitation of Comments, § 40.3 (Feb. 9, 2023), *available at* <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>; FDA, National Drug Code Directory (July 22, 2022), *available at* <https://www.fda.gov/drugs/drug-approvals-and-databases/national-drug-code-directory#:~:text=Marketing%20start%20date%20is%20the,no%20longer%20in%20commercial%20distribution>. With respect to the IRA’s Part B inflation rebate, CMS proposed to determine when a product is “marketed” by reference to the “date of first sale” that the manufacturer must report for ASP purposes, which likewise is an objective point-in-time determination. CMS, Medicare Part B Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1847A(i) of the Social Security Act, and Solicitation of Comments, § 50.3 (Feb. 9, 2023), *available at* <https://www.cms.gov/files/document/medicare-part-b-inflation-rebate-program-initial-guidance.pdf>.

²¹⁵ 83 Fed. Reg. 12,770, 12,784 (Mar. 23, 2018) (MDRP National Rebate Agreement); *see also* 42 CFR 447.502.

²¹⁶ CMS requires that Part D plan sponsor P&T committees “make a reasonable effort to review a new FDA approved drug product (or new FDA approved indication) within 90 days of its release onto the market and . . . make a decision on each new FDA approved drug product (or new FDA approved indication) within 180 days of its release onto the market, or a clinical justification will be provided if this timeframe is not met.” Prescription Drug Benefit Manual, ch. 6 § 30.1.5 (emphasis added).



CMS should not supplant wholesale the statute’s objective point-in-time “marketed” standard with an extra-statutory standard based on the Agency’s subjective judgment of sufficiency of utilization.²¹⁷ Such judgment is immaterial to whether a product is in fact marketed—i.e., is available to be bought and sold in the commercial marketplace.

Notably, Congress well knows how to statutorily impose a “bona fide” standard in the drug pricing context. Congress expressly established such a standard when amending the MDRP statute in 2010 to specify that only “bona fide” service fees are exempt from the calculation of AMP.²¹⁸ By contrast, Congress chose not to establish such a bona fide standard here. “[W]here Congress knows how to say something but chooses not to, its silence is controlling.”²¹⁹

CMS’s extra-statutory bona fide marketing standard has vast legal implications. For example, as noted above, the date on which CMS determines that a generic or biosimilar has been marketed determines when the MFP terminates.²²⁰ As such, through the bona fide marketing standard, CMS is effectively claiming for itself limitless discretion to prevent the MFP from timely (if ever) terminating, notwithstanding the fact that a generic or biosimilar has in fact come to market, based on the Agency’s subjective assessment of whether PDE data show that the generic or biosimilar is utilized sufficiently. In addition, CMS is implicitly claiming for itself authority to re-institute an MFP after an MFP has been terminated, if the Agency concludes based on PDE data that utilization of the generic or biosimilar ceases to be “robust and meaningful.”²²¹

Such policies are completely untethered to anything in the text or structure of the statute and run directly contrary to Congress’s intent to allow market-based competition to govern where a generic or biosimilar has come to market to compete with a drug or biologic.²²² The Agency’s approach is therefore patently unlawful. “[N]either federal agencies nor the courts can substitute their policy judgments for those of Congress.”²²³ CMS’s effort to do so here is “effectively the introduction of a whole new regime of regulation,” which “is not the one that Congress established.”²²⁴

The Agency’s unlawful standard also necessarily yields an inaccurate determination of when a generic or biosimilar was marketed. The Agency’s reliance on PDE data guarantees that there will be a time lag

²¹⁷ It is unclear, for example, whether CMS expects a generic or biosimilar to capture and maintain a certain percentage of the market.

²¹⁸ SSA § 1927(k)(1)(B)(i)(II) (as amended by Pub. L. No. 111–148, § 2503(a) (2010)).

²¹⁹ *Animal Legal Def. Fund v. U.S. Dep’t of Agric.*, 789 F.3d 1206, 1217 (11th Cir. 2015).

²²⁰ SSA § 1192(c)(2).

²²¹ See Initial Guidance at 67.

²²² See, e.g., SSA § 1192(c)(1).

²²³ *Brown & Williamson Tobacco Corp. v. FDA*, 153 F.3d 155, 176 (4th Cir. 1998), *aff’d*, 529 U.S. 120 (2000).

²²⁴ *MCI Telecomms. Corp. v. Am. Tel. & Tel. Co.*, 512 U.S. 218, 114 (1994).



between the actual date of marketing and the date of CMS's determination because it takes time for sales to be reflected in PDE data. Indeed, CMS's long-standing policy requiring Part D plan sponsors to determine whether to add a newly approved drug to their formulary within 180 days of its release onto the market ensures that the PDE data will not accurately reflect when the drug came to market. Many Part D plan sponsors will not add a newly approved drug to their formulary until the 180-day mark, and, thus, the first six months of PDE data following the market entry of the drug will necessarily reflect only very limited uptake.²²⁵ And some plan sponsors may choose not add the drug to their formulary at all. In addition, even where plan sponsors add the drug to their formulary, widespread uptake of a new product does not occur overnight. After a new product is made available for sale, providers and patients typically transition to such product gradually as they become increasingly familiar with its benefits relative to pre-existing alternatives.²²⁶ Such a product is in fact marketed during this uptake period, but CMS's standard ignores this fact and focuses instead on whether the product is adequately utilized, in contravention of the statutorily mandated standard.²²⁷ Such shifts in utilization patterns over time do not mean that the market is not working as intended.

The Agency compounds these concerns with its intent to review PDE data only once per month for purposes of determining when the MFP terminates.²²⁸ The Agency's approach virtually always ensures that there will be a lag between the actual date of marketing and the date of CMS's determination. This poses a significant concern with respect to when the MFP terminates. If there is a lag of even a single day between the actual date of marketing and the date of CMS's determination, a selected drug can be subject to the MFP for a full additional year. For instance, if, on April 1, a generic or biosimilar is in fact marketed on April 1, but CMS's determination of this fact is deferred until April 2, the selected drug is subject to the MFP for a full year longer than if CMS's determination had not been deferred.

It is imperative that CMS abandon its unlawful and ill-advised standard and instead adopt as its standard the "market date" reported under MDRP. The MDRP "market date" standard should be used for identifying *both* the date on which a generic or biosimilar is marketed *and* the date on which CMS determines that a generic or biosimilar has been marketed.

Under MDRP guidance, "market date" is "the earliest date the drug was first marketed under the application number by any labeler."²²⁹ Manufacturers report this date when reporting MDRP pricing

²²⁵ While plan enrollees may access a non-formulary drug via an exceptions process, access may not be immediate under such process; moreover, exception processes typically yield only a very small volume of utilization.

²²⁶ See A. Lubby, Factors affecting the uptake of new medicines: a systematic literature review, 14 BMC Health Services Research 469 (2014) (describing the various factors that affect early uptake of new medicines).

²²⁷ Other examples of deficiencies in CMS's approach include circumstances where low utilization is driven by uncontrollable factors such as supply shortages.

²²⁸ Initial Guidance at 62.

²²⁹ CMS, MDRP Data Guide § 5.15 (Apr. 2022).



data. As such, the MDRP “market date” is a familiar construct to both CMS and manufacturers, and carries the additional benefit of ensuring consistency across MDRP and the Negotiation Program. And, unlike the “date of first sale” used for ASP reporting purposes, the MDRP “market date” is available for generics and biosimilars without regard to whether they are subject to ASP reporting.²³⁰

It is particularly critical that the Agency equate the date on which CMS determines that a generic or biosimilar has been marketed with the MDRP “market date” because, as noted above, the difference of a single day in the date of CMS’s determination can result in the MFP being extended for a full additional year. Failing to do so would have a dramatic chilling effect on the development of generics and biosimilars. Manufacturers would be seriously disincentivized against investing in the development of such products if there is a risk that they would be forced to compete with the MFP for an unduly extended period of time. This, in turn, would defeat Congress’s objective of encouraging the development of generic and biosimilar market competitors.

For all of these reasons, we strongly oppose CMS’s extra-statutory bona fide marketing standard, and strongly urge CMS instead to adopt the MDRP “market date” as a uniform standard for identifying both the date on which a generic or biosimilar is marketed and the date on which CMS determines that a generic or biosimilar has been marketed.

VII. Other Issues

A. Selected Drugs and Inflation Rebates

BIO urges CMS to clarify that selected drugs are not subject to an inflation rebate.

In its Initial Guidance, CMS solicits comment on the application of Part B and Part D inflation rebates to selected drugs.²³¹ Notably, CMS asserts: “The Part B and Part D inflation rebate programs apply to selected drugs, regardless of the status of the drug as a selected drug. Alternatively said, whether a drug is a selected drug will have no bearing as to whether the drug is also subject to the Part B and Part D inflation rebate programs.”²³² This assertion is incorrect. BIO asks CMS to clarify a selected drug is not subject to an inflation rebate.

²³⁰ The “date of first sale” is reported only for products subject to ASP reporting, and thus may not be available for all generics and biosimilars whose marketing is implicated by the Negotiation Program. By contrast, the “market date” reported under MDRP is more broadly reported and is thus the superior metric to use. See CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1860D-14B of Social Security Act, and Solicitation of Comments, (Feb. 9, 2023), <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>.

²³¹ Initial Guidance at 71.

²³² *Id.*



By statute, the Part B inflation rebate calculation is based in relevant part on the amount by which “106 percent of the amount determined under paragraph (4) of [section 1847A(b) of the SSA] for [a part B rebatable drug] during the calendar quarter . . . exceeds . . . the inflation-adjusted payment amount . . . for such part B rebatable drug during the calendar quarter.”²³³

Importantly, the circumstances under which an amount is “determined” under paragraph (4) is dictated by section 1847A(b)(1) (paragraph (1)).²³⁴ Specifically, paragraph (1) dictates a payment amount of, “in the case of a single source drug or biological . . . , 106 percent of the amount determined under paragraph (4) or in the case of such a drug or biological product that is a selected drug . . . , with respect to a price applicability period . . . , 106 percent of the maximum fair price . . . applicable for such drug and a year during such period.”²³⁵

In other words, the payment amount for a selected drug is determined under paragraph (1), and such payment amount is determined without regard to paragraph (4). Rather, it is only the payment amount for a non-selected drug that is determined under paragraph (4).

It necessarily follows that the Part B inflation rebate calculation has no application to a selected drug. With respect to such a drug, there is no amount “determined under paragraph (4),” and therefore Part B inflation rebates have no applicability.

This is not surprising. There is no policy reason for Congress to apply inflation rebates to selected drugs. A manufacturer should not be obligated to pay an inflation rebate on a selected drug because Medicare expenditures on a selected drug are already constrained by the maximum fair price.²³⁶ Thus, with respect to a selected drug, Medicare is shielded from the increase in expenditures occasioned by a price increase that outpaces inflation that an inflation rebate is intended to address. Medicare does not need to be made whole on account of such a price increase, and, thus, no inflation rebate should be due.

For all of these reasons, CMS should clarify that a selected drug is not subject to an inflation rebate.

²³³ SSA § 1847A(i)(3) (emphasis added).

²³⁴ See *id.* § 1847A(b)(1).

²³⁵ *Id.* § 1847A(b)(1)(B) (emphasis added).

²³⁶ *Id.* §§ 1847A(b)(1)(B); 1860D-2(d)(1)(D).



B. MFP and ASP

BIO urges CMS to amend its regulatory definition of “unit” to exclude MFP units from the ASP calculation.

By statute, MFP units are included in Best Price.²³⁷ Sales included in Best Price are also generally included in ASP.²³⁸ Thus, in the ordinary course, MFP units would be included in the ASP calculation. But the inclusion of MFP units in the ASP calculation would have vast and dire consequences for patient access.

The inclusion of MFP units in the ASP calculation would increasingly deflate ASP over time. As a result, ASP-based provider reimbursement would increasingly become inadequate to cover providers’ acquisition costs. Eventually, providers would be left financially underwater if they were to furnish a selected drug to an MFP-ineligible individual, creating a very real risk that providers would no longer furnish such drugs to such individuals. And this vital threat to patient access to necessary medicines would be far-reaching. ASP is a reimbursement benchmark commonly used by non-Part B payers with respect to Part B drugs. As such, although Part B reimbursement for selected drugs will not be based on ASP, this would negatively affect countless individuals insured by non-Part B payers.

Fortunately, CMS has clear legal authority to prevent this. The ASP statute unambiguously confers on CMS broad authority to define “unit” for purposes of the ASP calculation “as . . . [CMS] determines appropriate.”²³⁹ CMS undoubtedly may exercise such authority to exclude MFP units from the ASP calculation to avoid the patient access concern described above.

The legislative history of the ASP statute makes abundantly clear that Congress intended for CMS to exercise such discretion in this way in precisely this sort of circumstance. When Congress delegated CMS the authority to define “unit” for purposes of the ASP calculation, it specifically stated that it was doing so to allow for the exclusion of “those sales that do not reflect market prices” from ASP.²⁴⁰ By definition, MFP units do not reflect market prices.

There is also clear Agency precedent for excluding units that do not reflect market prices from the ASP calculation. In 2005, CMS carved Competitive Acquisition Program (CAP) units out of the ASP exclusion by excluding such units from the “unit” definition.²⁴¹ In doing so, CMS noted that ASP and CAP prices

²³⁷ *Id.* § 1927(c)(1)(C)(ii)(V).

²³⁸ *See id.* § 1847A(c)(2)(A); *see also* 42 C.F.R. § 414.804(a)(1), (4)(i).

²³⁹ SSA § 1847A(b)(2)(B).

²⁴⁰ *See* H.R. Rep. No. 108-391, at 587–88 (2003).

²⁴¹ 70 Fed. Reg. 39,021, 39,077 (Jul. 6, 2005); *see also* 74 Fed. Reg. 61,738, 61,915 (Nov. 25, 2009).



were “intended to be alternatives to each other” and, thus, CAP units should not be included in the ASP calculation.²⁴²

Identical reasoning supports excluding MFP units from the ASP calculation. MFP units do not reflect market prices: Rather, the MFP is a government-set price. Further, the MFP functions as an alternative to ASP: Part B will reimburse providers based on the MFP in lieu of ASP.²⁴³

For all these reasons, sound policy dictates that CMS exclude MFP units of selected drugs from the ASP calculation. BIO urges CMS to do so well in advance of the first IPAY to avoid any confusion and potential destabilization on non-Medicare markets once MFPs go into effect for the first set of selected drugs.

C. Civil Monetary Penalties (CMPs)

BIO urges CMS to proceed with caution on the implementation of CMPs as proposed given the ambitious timelines in the statute and to allow manufacturers a reasonable time period to cure deficiencies before CMPs are imposed. And in no case should the Agency impose a CMP prior to finalization of relevant regulations.

Under the IRA, CMS can impose CMPs on drug manufacturers for the following infractions related to the Part D Drug Negotiation program:

- **Refusing Access to MFP Price:** CMS will impose a CMP of 10 times the amount equal to number of units of drug furnished multiplied by the difference between the price for such drug made available to MFP-eligible entities on a Primary Manufacturer of a selected drug that has entered into an Agreement with CMS and fails to provide access to a price that is less than or equal to the MFP to MFP-eligible individuals dispensed the selected drug to pharmacies, mail order services, or other dispensers with respect to MFP-eligible individuals who are dispensed the selected drug or to hospitals, physicians, or other providers or suppliers that furnish or administer the selected drug to MFP-eligible individuals.
- **Failure to Comply to Requirements:** Any Primary Manufacturer of a selected drug that has entered into an Agreement with that fails to comply with requirements determined by CMS to be necessary for the purposes of administering the Negotiation Program and monitoring

²⁴² 78 Fed. Reg. at 61,915.

²⁴³ SSA § 1847A(b)(1)(B).



compliance with the Negotiation Program will be subject to a CMP of \$1,000,000 for *each day* of such violation.

- **Provision of False Information:** If CMS determines that any manufacturer knowingly provides false information under the procedures to apply the aggregation rule for the Small Biotech Exception, such manufacturer shall be subject to a CMP equal to \$100,000,000 for each item of such false information. Likewise, if CMS determines that any Biosimilar Manufacturer knowingly provides false information under the procedures to apply the aggregation of the Biosimilar Delay, the manufacturer shall be subject to a CMP equal to \$100,000,000 for each item of such false information.

CMS will provide notice to the manufacturer with information regarding the CMP in accordance with section 1128A of the Act, including the option to either pay the CMP or to request a hearing as outlined in section 1128A. The CMP notice will include: Basis for the CMP; CMP amount due; Deadline for the manufacturer to respond with a hearing request or submit the CMP payment; Method to submit CMP payment(s); and Information on the right to request a hearing

The manufacturer will have 60 days from the date of receipt of the CMP notice to request a hearing—If the manufacturer does not request a hearing within 60 days, the CMP will be considered due on day 60 following the date of receipt of the CMP notice.

BIO urges CMS to proceed with caution on the implementation of CMPs as proposed. By any recognition, the time frames in statute for implementation of myriad sweeping changes in multiple parts of the Medicare program are ambitious. To make analogies to another program, BIO reminds CMS that a final rule to impose CMPs on drug manufacturers as part of the 340B program in 2017 was delayed multiple times. Although the 2017 Final Rule was scheduled to take effect on March 6, 2017, HRSA delayed the implementation of the rule multiple times. The Agency ultimately postponed the effective date of the rulemaking until July 1, 2019, to allow for “necessary time to consider more fully the substantial questions of fact, law, and policy identified by the Department during its review of the rule.”

We similarly urge CMS to proceed cautiously with the imposition of CMPs on drug manufacturers and urge all stakeholders to work in good faith to comply with the statutory requirements of data reporting. To this end, we request that CMS send a notice of intent to impose a CMP and a reasonable period to cure the deficiency and/or to dispute the basis for the CMP, before any imposition of a CMP. The IRA imposes a tremendous amount of data reporting on drug manufacturers and puts them at risk for significant financial penalties. It will take time for manufacturers, especially small manufacturers, to comply in good faith with all the necessary data collection requests in the first years of the Negotiation program. And in no case should the Agency impose a CMP prior to finalization of relevant regulations.



D. Negotiation Program Agreement

BIO urges CMS to ensure that the text of the Negotiation Program Agreement is made available for public comment at least sixty days in advance of the first selected drug publication date. Further, CMS should abandon its “Primary Manufacturer” and “Secondary Manufacturer” construct as part of the Agreement as it is impracticable and has no legal basis.

The Initial Guidance states that the Agency will make “reasonable efforts” to make the final text of agreement available to the public before the first selected drug publication date.²⁴⁴ It is imperative that CMS make the text of the agreement available for public comment and do so well in advance of when manufacturers will be required to execute the agreement.

Advance notice of, and an opportunity comment on, the precise content of the Negotiation Program Agreement is vital because manufacturers are subject to CMPs of \$1 million dollars per day for a violation of a terms of the agreement.²⁴⁵ What is more, manufacturers that decline to enter into the Negotiation Program Agreement are subject to punitive excise taxes, such that manufacturers are effectively compelled to enter into the agreement.²⁴⁶ Under these circumstances, it is imperative that CMS provide advance notice of, and an opportunity to comment on, the exact terms of the Negotiation Program Agreement. Manufacturers must be reasonably apprised of the specific obligations to which CMS proposes they be subject, and have reasonable opportunity to comment thereon, when compliance is enforced via such extraordinary sanction.

Advance notice is necessary at a minimum because manufacturers may need lead time to establish new processes in order to be prepared to comply with the terms of the agreement. CMS cannot put manufacturers in the untenable position of being subject to sanction for failing to comply with requirements that they cannot fulfill because the Agency did not supply adequate advance notice. Courts have long recognized that “[i]mpossible requirements imposed by an agency are perforce unreasonable” and therefore arbitrary and capricious.²⁴⁷

We also reinforce our earlier comments regarding CMS’s proposal to hold a “Primary Manufacturer” responsible for submitting applicable information concerning a “Secondary Manufacturer.” CMS also proposes, among other things, to require that “Primary Manufacturers” ensure that “Secondary Manufacturers” make the MFP available to MFP-eligible entities individuals and other entities, and CMS would impose CMPs on “Primary Manufacturers” for noncompliance by “Secondary Manufacturers.” We

²⁴⁴ Initial Guidance at 27.

²⁴⁵ SSA § 1197(c).

²⁴⁶ IRC § 5000D(b)(1)(A).

²⁴⁷ *All. for Cannabis Therapeutics v. DEA*, 930 F.2d 936, 940 (D.C. Cir. 1991).



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urge CMS to abandon its proposed requirements under this “Primary Manufacturer” and “Secondary Manufacturer” construct. A Primary Manufacturer has no inherent legal authority to compel a Secondary Manufacturer to act or not act.

E. Patient Access and Part D Plan Formulary Placement

CMS should take steps to protect patient access to needed therapies in all Medicare Part D Plans.

By statute, Part D plans must place selected drugs on their formularies.²⁴⁸ BIO recommends that CMS clarify how it will ensure robust beneficiary access to needed therapies, including selected drugs, and asks CMS to ensure safeguards that allow for diversity across formularies to meet patient needs. CMS should try to minimize class effects from the MFP process that would result in narrower formularies and provide fewer choices to patients. In addition, CMS should monitor plan coverage and tiering design, clinical appropriateness of utilization management policies, cost-sharing levels, and patient out of pocket exposure. BIO encourages CMS to update its oversight of formulary requirements and to re-examine Part D coverage determinations and appeals as well as tiering exceptions.

BIO appreciates this opportunity to provide feedback to CMS on the Initial Guidance. We look forward to continuing to work with the Agency on these important issues. Should you have any questions, please do not hesitate to contact Crystal Kuntz at 202-962-9200 or Ckuntz@bio.org.

Sincerely,

/s/

John Murphy
Chief Policy Officer

A handwritten signature in blue ink, appearing to read 'John Murphy'.

/s/

Crystal Kuntz
Vice President, Healthcare Policy & Research

A handwritten signature in blue ink, appearing to read 'Crystal Kuntz'.

²⁴⁸ *Id.* § 1860D-4(b)(3)(I).

Congress of the United States
Washington, DC 20515

April 12, 2023

The Honorable Xavier Becerra
Secretary
Department of Health and Human Services
200 Independence Avenue, SW
Washington, D.C. 20201

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Dear Secretary Becerra and Administrator Brooks-LaSure:

We write to express disappointment and concern with recent implementation guidance for the drug price-setting provisions included in the Inflation Reduction Act (IRA, Pub. L. 117-169). This guidance exacerbates the law's statutory flaws and compounds the profound uncertainty and risk posed by the legislation's sweeping drug price controls. We encourage you to reconsider the many components of the initial guidance that will otherwise stifle medical innovation and quality improvement, discourage proven public-private partnerships, undermine American intellectual property (IP) protections, and provide unacceptable conditions for public feedback. If finalized as proposed, these provisions will serve to make bad policy worse, harming patients, caregivers, and health care providers across the United States for generations to come.

The Administration's guidance clearly values government power and overreach above precedent and statute, at the expense of patients seeking potentially life-saving treatments. In an apparent effort to subject as many medications as possible to the IRA's price-setting program, the guidance uses an unusual definition of "qualifying single-source drugs" that aggregates entirely different medications according to their active ingredient or moiety, thereby discouraging research into future drug indications. This approach will blunt incentives for meaningful product improvements, in addition to punishing products that treat more than one disease.

The Centers for Medicare and Medicaid Services' (CMS) misguided drug definition will chill efforts to mitigate side effects, improve adherence, bolster quality, and identify new uses and patient populations that might benefit from a given product. As outlined by Professor Erika Lietzan in a 2018 study, "Development of new uses for already approved drugs, in particular, can make profound contributions to the public health."¹ Another analysis, released that same year, details a lengthy list of examples along these lines, such as a "failed attempt to a cancer drug" repurposed decades later to become "the first breakthrough in AIDS therapy."² By reducing complex drugs and biologics to their active ingredients and collapsing new drug applications into a single product for price-setting purposes, the definition included in CMS' guidance will decrease the likelihood of these types of groundbreaking developments moving forward. In light

¹ https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3103293

² <https://www.liebertpub.com/doi/pdf/10.1089/blr.2018.29073.cmh>

of this risk, we urge CMS to adopt a more conventional definition with a credible basis in the statute.

Even more alarmingly, this guidance appears to serve as a backdoor mechanism for achieving partisan policy goals, to the detriment of Americans' health care. Specifically, the guidance treats federal financial support at any stage of drug discovery or development as grounds for further price manipulation by the Secretary under the program, resulting in a de facto expansion of so-called "march-in" authority, as referenced, but never imposed, under the Bayh-Dole Act. This effort comes despite consistent rejections, including by the Biden Administration,³ of attempts to rely on federal funding for a drug as grounds to impose price controls.⁴ In fact, the Bayh-Dole Act's bipartisan authors repeatedly affirmed that their framework aimed to incentivize public-private partnerships and accelerate access to meaningful medical innovations, rather than to discourage such collaborations or to punish innovators and research centers through pricing restrictions.⁵ The price-setting program's treatment of federal support risks undercutting private-sector interest in partnering with the government, further harming American patients.

Anti-innovation policymaking pervades the agency's initial guidance. Drugs with longer remaining patent terms or exclusivities, for instance, will see a downward adjustment in their Secretary-mandated prices, inverting the IP incentive structure that has driven most major inventions and breakthroughs since our nation's founding. Research and development costs, meanwhile, would receive insufficient consideration during the price-setting process, with a narrow definition that ignores the complexities of drug development. In this way, CMS perpetuates a troubling pattern of mission creep, whereby the agency bypasses Congress and other federal departments to pursue goals outside of its jurisdiction.^{6, 7}

In addition to these and other substantive policy concerns with the Administration's drug price-setting program, we also urge CMS to incorporate meaningful transparency and accountability into every stage of the new initiative's implementation. Already, we find the opportunity for public comment and its unduly brief response period leaving patients, caregivers, and other stakeholders inadequate time and opportunity to review and consider the vast new government rules and regulations at stake. CMS should provide longer comment periods and should not attempt to shield any portions of its regulatory proposals from public feedback or engagement. Furthermore, in implementing the price-setting program, the agency has an obligation to extend offers for additional meetings to hear feedback and input directly from those subjected to or otherwise affected by the process. For any number of conditions, from Alzheimer's disease and cancer to the 95 percent of rare diseases that currently lack an approved treatment option, CMS must also ensure that patients can play a proactive and consistent role in the decision-making process.

Additionally, we have major concerns with the guidance's severe limitations on basic due process protections, including for small businesses. The proposed policies would prohibit the

³ <https://www.keionline.org/wp-content/uploads/NIH-rejection-Xtandi-marchin-12march2023.pdf>

⁴ <https://www.aamc.org/media/61966/download?attachment>

⁵ <https://www.washingtonpost.com/archive/opinions/2002/04/11/our-law-helps-patients-get-new-drugs-sooner/d814d22a-6e63-4f06-8da3-d9698552fa24/>

⁶ https://www.finance.senate.gov/imo/media/doc/crapo_letter_to_cms_on_final_coverage_decision.pdf

⁷ https://www.finance.senate.gov/imo/media/doc/letter_on_medicare_and_accelerated_approval.pdf

disclosure of materials sent by the agency during the price-setting process, and manufacturers would ultimately need to destroy any such information, effectively undercutting the potential for the predictability, precedent, and stability that govern virtually all adjudication processes. When coupled with the law's broad restrictions on judicial and administrative review, these proposals stifle any opportunity for accountability, program integrity, or recourse for aggrieved parties.


We urge you to work diligently and quickly to address these and other issues as you begin implementing this far-reaching new price control program. The preliminary decisions made through this initial guidance process, if carried out without greater reflection and input from the public, will have dire consequences for American patients for decades to come.

If you have questions about this request, please contact Conor Sheehy of the Senate Finance Committee staff, Alec Aramanda of the House Committee on Energy and Commerce, and Patrick Dumas of the House Committee on Ways and Means.

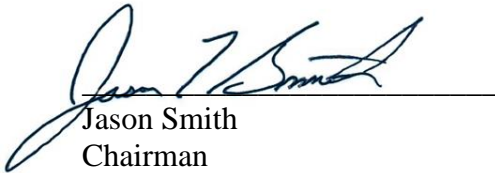
Sincerely,



Mike Crapo
Ranking Member
Committee on Finance



Cathy McMorris Rodgers
Chair
House Committee on Energy and Commerce



Jason Smith
Chairman
House Committee on Ways and Means



April 11, 2023

Ms. Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services (CMS)
Washington, D.C.
Via email: IRAREbateandNegotiation@cms.hhs.gov
Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

We applaud the Centers for Medicare and Medicaid Services for soliciting feedback on the draft program guidance issued to describe the implementation of Medicare drug price negotiation under the Inflation Reduction Act. Since 1999, the Connecticut Health Policy Project (www.cthealthpolicy.org) has worked to improve access to affordable, quality healthcare for everyone. We provide policymakers and the public with analysis of policy options to achieve those goals. We have worked for years to protect underserved populations, including patients with disabilities, from discrimination. We are especially concerned about financial access to critical medications for underserved and at-risk populations such as the elderly, disabled, and people with complex medical needs. Currently, the prices of essential, innovative medications are the greatest barrier to accessing both the medications and, by raising premiums and cost sharing, the affordability of coverage for everyone. Finally having the authority to negotiate fair drug prices for seniors in the Medicare program is a critically important step in meeting the goals of a just health care system.

In order to ensure that drug prices are fair for consumers, we need independent analysis and tools that can be leveraged to determine what a fair drug price is. It is imperative to objectively compare treatments for clinical effectiveness and affordability using well-vetted, evidence-based tools. Given our strong and sustained advocacy for underserved communities, we support CMS being able to use such independent analyses, specifically cost-effectiveness.

We note that your program guidance requests information on metrics that “may treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill and that CMS should also exclude from consideration when developing offers and reviewing counteroffers.” It is imperative that CMS retain the ability to use measures of cost-effectiveness that do not undervalue the life extension of people we serve including those with disabilities, those who are older, or those who are terminally ill. Therefore, we encourage CMS to use nondiscriminatory health measures and versions of cost-effectiveness analysis to help CMS develop offers and review counteroffers under the IRA. Specifically, we believe that

measures that value each year of extended life the same meet the intent of the statute and do not “treat extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.” Examples of such non-discriminatory measures include the equal value of life years gained (evLYG), health years in total (HYT), or the generalized risk adjusted quality-adjusted life year (GRA-QALY).

Prescription drug prices are driving up healthcare costs that are squeezing family, employer, and government budgets -- displacing other healthcare spending and other important priorities beyond health. Over [one in ten US households](#) couldn't pay for a prescription drug due to cost. More than [five million Medicare beneficiaries](#) struggle to afford medications. While unintended, high drug prices ultimately undermine the health of patients.

Again, we applaud CMS for taking this important step, through negotiation, to ensure seniors have access to fairly-priced drugs.

Thank you for your commitment to the health and affordability of care for all Americans.

Sincerely,

A handwritten signature in cursive script that reads "Ellen M. Andrews". The signature is written in dark ink and is positioned above the typed name and title.

Ellen Andrews, PhD
Executive Director
Connecticut Health Policy Project
andrews@cthealthpolicy.org

April 13, 2023

Submitted via email to: IRAREbateandNegotiation@cms.hhs.gov

Meena Seshamani, M.D., Ph.D.,
CMS Deputy Administrator & Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health & Human Services
P.O. Box 8013
Baltimore, MD 21244-8013

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear. Dr. Seshamani:

CVS Health appreciates the opportunity to provide comments on “Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments” (“Initial Guidance”) issued by the Centers for Medicare & Medicaid Services (CMS) on March 15, 2023.¹

CVS Health serves millions of people through our local presence, digital channels, and our nearly 300,000 dedicated colleagues – including more than 40,000 physicians, pharmacists, nurses and nurse practitioners. Our unique health care model gives us an unparalleled perspective on how systems can be better designed to help consumers navigate the health care system – and their personal health care – by improving access, lowering costs, and being a trusted partner for every meaningful moment of health. And we do it all with heart, each and every day.

We thank CMS for giving the public and stakeholders an opportunity to provide input on various aspects of the Initial Guidance. Implementation of the Medicare Drug Price Negotiation Program (Program) will be complex and challenging, and will affect not only beneficiaries and manufacturers, but every entity in the pharmaceutical supply chain. Given our role as a health plan, health care provider, pharmacy and pharmacy benefits manager, we are well-positioned to comment from different perspectives to help facilitate the smooth implementation of the Program.

We especially appreciate CMS’ making clear that it is the responsibility of the Primary Manufacturer to ensure that the maximum fair price (MFP) is made available to MFP-eligible individuals as well as to pharmacies, mail order services, and other dispensers that provide a selected drug to an MFP-eligible individual. We also appreciate CMS clarifying its intention that its agreement with the Primary Manufacturer would not restrict the Primary Manufacturer or Secondary Manufacturer(s) from offering a price lower than the MFP. We ask that CMS implement the Program in such way that not only allows for manufacturers to offer lower prices, but continues to encourage them to do so. The primary mechanism used today to incentivize manufacturers to offer lower prices in the Part D program is inclusion and placement on a Part

¹ Available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

D plan's formulary. Therefore, it is critical that CMS implement the Program in a manner that not only preserves, but strengthens this mechanism by giving Part D sponsors and their PBMs maximum flexibility to determine which drugs, and for selected drugs, which dosage form(s) and strength(s), to include on their formularies.

We also strongly support the requirement in the Initial Guidance that a Primary Manufacturer ensure that pharmacies, mail order services, and other dispensers, as well as intermediate entities, such as wholesalers, as applicable, are reimbursed timely for the full amount of the difference between their acquisition cost for the selected drug and the MFP within 14 days. We assume that the 14 day period refers to 14 calendar days after a request for reimbursement is received by the Primary Manufacturer, but ask that CMS clarify this in the Initial Guidance. We agree with CMS that existing mechanisms can be leveraged for this purpose, including use of the unique Part D processor identification number (RxBIN) and Part D processor control number (RxPCN) combination used by PBMs, to identify a claim for a MFP drug paid under a Medicare Part D benefit.

However, it is important to recognize that the Program differs from existing programs, such as the coverage gap discount program (CGDP), in significant respects. These differences will require that new processes be built and implemented, and this will involve significant resources and risk for participants in the pharmaceutical supply chain. For example, unlike the CGDP, which involves only point-of-sale adjustments, the Program will require reconciliation to dispensers' acquisition costs, something that is not currently in place in the industry. In light of this, we recommend that CMS seek ways in which to streamline and facilitate the process as much as possible, such as through the development of standardized agreements and reporting formats to be used by manufacturers and others in the supply chain to implement the Program. We also recommend that CMS require Medicare D Part D claims impacted by MFP be clearly identified with the applicable basis of reimbursement code value as defined by the National Council of Prescription Drug Programs.

CMS proposes two ways in which the primary manufacturer can ensure that access is provided to the MFP, namely, (1) ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP; or (2) providing retrospective reimbursement for the difference between the dispensing entity's acquisition cost and the MFP. Given that the MFP is required to be made available only to Part D enrollees and dispensers will not know ahead of time how many patients will be eligible for the MFP, we anticipate that the second method -- retrospective reimbursement of the difference between the dispensing entity's acquisition cost and the MFP-- will in most cases be used. However, since acquisition cost data is highly sensitive competitive data, dispensers and others in the supply chain are unlikely to be willing to share this directly with manufacturers or their vendors that are involved in the supply chain. This creates a conflict of interest or, at least, competing business interests.

In order to address this, we believe it may be necessary to establish a chargeback system between each entity in the supply chain and the entity from which it purchased the drug. So, for example, in most cases pharmacies will seek reimbursement from the wholesaler from which they purchased the drug, and wholesalers in turn will seek reimbursement from the manufacturer from which it purchased the drug. This will require reporting by the dispenser of MFP drugs dispensed to MFP-eligible individuals during a given period. To the extent this reporting can be standardized and aggregated across manufacturers, it will reduce the costs and burdens on dispensers and others in the supply chain. In addition, many technical issues will need to be addressed, such as accounting for partial dispensed quantities to the full

package quantity. We ask that CMS provide ongoing guidance as these issues are worked through.

CMS states that it anticipates that pharmaceutical database companies will publish the MFPs so that the amounts would become more readily accessible to pharmaceutical purchasers, and CMS asks for comments on additional ways that CMS could help dispensing entities and MFP-eligible individuals know the MFP for a selected drug. We recommend that promptly after the MFP is established, Primary Manufacturers be required to report the MFP and its effective date to the standard drug compendia vendors and that these prices be made available in existing drug files incorporated into provider and payer claim adjudication systems.

Finally, we appreciate CMS confirming that dispensers will be paid a dispensing fee in addition to the MFP. We ask that CMS also confirm that this dispensing fee not only may, but should, be higher to ensure that pharmacies receive fair compensation for dispensing MFP drugs. The Program will only be a success if all entities in the supply chain are treated fairly and compensated appropriately for their services.

Thank you for considering our comments. We understand that the smooth and effective implementation of the Program is a top priority of CMS and Congress as a means to control drug costs. We stand ready to help CMS in any way we can to make the Program work and achieve its goals.

We would be happy to respond to any follow-up questions you may have.

Sincerely,

A handwritten signature in dark ink, appearing to read "Melissa Schulman". The signature is fluid and cursive, with the first name "Melissa" and last name "Schulman" clearly distinguishable.

Melissa Schulman
Senior Vice President, Government & Public Affairs
CVS Health



April 14, 2023

The Honorable Xavier Becerra
Secretary of Health and Human Services
U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

The Honorable Chiquita Brooks-LaSure
Administrator Centers for Medicare and Medicaid Services
U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Secretary Becerra and Administrator Brooks-LaSure:

The Cystic Fibrosis Foundation is a national organization dedicated to curing cystic fibrosis (CF). We invest in research and development of new CF therapies, advocate for access to care for people with CF, and fund and accredit a network of specialized CF care centers. We thank the Centers for Medicare and Medicaid Services (CMS) for the opportunity to provide comments on the initial Medicare Drug Pricing Negotiation Program Guidance.

Cystic fibrosis is a life-threatening genetic disease that affects close to 40,000 children and adults in the United States. CF causes the body to produce thick, sticky mucus that clogs the lungs and digestive system, which can lead to life-threatening infections. If left untreated, infections and exacerbations caused by CF can result in irreversible lung damage, and the associated symptoms of CF lead to early death, usually by respiratory failure. Through thorough, aggressive, and continuously improving disease management, the average life expectancy for people with cystic fibrosis has risen steadily over the last few decades. With recent advancements in treatment options, more people with CF are aging onto Medicare than ever before.

We provide the following comments and recommendations for future guidance and program implementation.

Orphan Drug Exclusion

The CF Foundation appreciates CMS's request for recommendations to preserve and support incentives for orphan drug development within the context of Medicare drug price negotiation. However, we are concerned that the orphan drug exclusion as worded in section 30.1.1 of this guidance ("designated as a

drug for only one rare disease or condition”) may have concerning implications for development in this space.

Specifically, limiting the exclusion to drugs that have only one orphan designation may disincentivize sponsors from performing comprehensive research on drugs with the potential to treat multiple rare diseases, which we do not believe was the intent of this provision in the Inflation Reduction Act (IRA). Because orphan drug designations for new drugs are requested before submission of a marketing application and include tax credits for clinical research expenses, sponsors frequently request them very early in the drug development process. Having a single orphan designation as a criterion for exclusion from price negotiation may therefore disincentivize sponsors from pursuing concurrent development programs for drugs that may initially hold promise for treating multiple rare diseases or conditions.

We believe Congress intended to tailor this exclusion to drugs that are exclusively *approved* to treat rare disease populations and did not intend to deter sponsors from investigating a given therapy for multiple orphan diseases. We therefore urge CMS to clarify that drugs that receive multiple orphan drug designations will still be eligible under this exclusion.

Clinical Benefit

The CF Foundation appreciates CMS’s commitment to incorporating data beyond clinical trials to demonstrate the clinical benefit of a therapy. Using data beyond clinical trials, including patient-reported outcomes and real-world evidence, is critical to understanding the full value of therapies. In CF, benefits for patients who are on transformative modulator therapies extend far beyond the endpoints measured in clinical trials. For instance, real-world data has shown a reduction in the number of lung transplants and reduced treatment burden for patients on modulator therapy – benefits not captured in randomized clinical trials.

We support CMS recognizing that Quality Adjusted Life Years (QALYs) should not be used as a primary measure of cost-effectiveness analyses. QALYs look solely as longevity and do not account for the patient experience and benefits outside of those directly related to the length of life.

When CMS consults subject matter experts, this should include members of the patient community. Clinical experts, drug manufacturers, and researchers may not fully grasp the benefits or complications of a given therapy for patients. For instance, those individuals do not necessarily understand issues like treatment burden, which is an important consideration for people with CF. Additionally, in order to obtain meaningful feedback and data, we recommend CMS simplify and update the feedback submission form with plain language, provide significant notice of data collection prior to the 30-day submission timeframe, and issue specific instructions on the standardized format needed for data submitted. These updates will make it more likely for patients to engage, particularly given the short statutory timelines.

Data Collection on Impact

We support the provisions that require negotiated products to be included on Medicare Part D formularies. In order to evaluate the long-term impacts of the IRA and drug price negotiations on patient access and cost, we recommend CMS implement a data collection and analysis system looking at impacts both across a manufacturer’s drug portfolio, Part D plans, and in other insurance markets (marketplace, Medicare Advantage, and commercial plans). This should include drug expenditures to identify cost-shifting from a MFP product to a non-negotiated product, and trends in utilization and health outcomes.

Bethesda Office

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301.951.4422 800.FIGHT.CF Fax: 301.951.6378
www.cff.org email: info@cff.org

The CF Foundation appreciates the opportunity to provide comments on this initial guidance. We look forward to working with CMS on these critical issues to ensure access and affordability for people with CF.

Sincerely,

A handwritten signature in black ink, appearing to read 'Mary B. Dwight', with a stylized, cursive script.

Mary B. Dwight
Chief Policy & Advocacy Officer
Senior Vice President, Policy & Advocacy
Cystic Fibrosis Foundation

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April 11, 2023

Via Electronic Delivery

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Cytek Biosciences (NASDAQ: CTKB) appreciates the opportunity to comment on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare and Medicaid Services (“CMS”) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

Cytek Biosciences provides cell analysis tools that facilitate scientific advances in biomedical research, drug discovery and development, and clinical applications. Our products are used at many of the world’s most renowned biotech and pharmaceutical companies, CRO firms, and government and academic research institutions.

There are multiple provisions in the IRA with negative unintended consequences for drug development, treatment cost, and availability:

1. Fewer new drugs will be developed – not only for seniors, but also for all Americans – if small molecule drug price negotiations begin at 9 years instead of 13 years.
2. Ironically, treatment costs will likely increase as the list of available therapies shifts away from small molecules and toward biologics, thereby frustrating the intent of the Inflation Reduction Act
3. Fewer repurposed drugs will be available to treat additional orphan medical conditions beyond the original approval population if price negotiation is initiated at 9 years for small molecule drugs as well as biologics.
4. Fewer new drugs will be developed unless CMS uses broadly defined criteria for assessing the value a new drug can bring in comparison to the therapeutic alternatives it considers when proposing negotiated Medicare prices. These criteria should include efficacy, safety, ease-of-use, value to caregivers, and risk reduction to the remaining population.
5. The “bona fide” generic competition standard will result in fewer new generics and higher costs for old drugs by reducing the reward for first filer generics and harming generic

competition. CMS should rely on competitive market derived prices rather than its negotiation process in setting drug prices.

6. The criteria used to assess a drug's value must be made public to allow companies to focus scarce resources on developing drugs that will actually be used clinically rather than wasting resources on projects that will be terminated due to lack of investment return. Wasting resources in this manner prevents the development of drugs that otherwise could have brought benefit to patients.

There are a variety of reasons for these consequences, which Cytex would be pleased to discuss with CMS, along with effective solutions that will address the real intent of the IRA legislation.

Please contact Paul Goodson, Head of Investor Relations, at 442-888-3854, or pgoodson@cytekbio.com, if we can support CMS in this important mission.

Sincerely,

Wenbin Jiang, Ph.D.
Chairman and CEO
Cytex Biosciences, Inc.



April 14, 2023

VIA Electronic Filing – IRAREbateandNegotiation@cms.hhs.gov

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attn: PO Box 8016

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Seshamani:

Daiichi Sankyo, Inc. submits the below comments in response to the Centers for Medicare & Medicaid Services' (CMS) *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (Guidance).¹ Daiichi Sankyo is dedicated to creating new modalities and innovative medicines for patients around the globe. With more than 100 years of scientific expertise, our company draws upon a rich legacy of innovation and a robust pipeline of promising new medicines to help patients. Through the outstanding knowledge and commitment of our scientists and other employees, we create innovative new medicines and methods of drug discovery and delivery. We share a passion for innovation, as well as compassion for the patients who need our medicines.

Daiichi Sankyo is disappointed that CMS is not accepting comments on Section 30 of the Guidance, which includes CMS' identification of a "qualifying single source drug" (QSSD), a fundamental component of the "Negotiation Program" (Program), and that this may raise due process and other issues. Daiichi Sankyo is encouraged, however, by CMS' stated interest in implementing the Program to

¹ Guidance, available at [Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments \(cms.gov\)](https://www.cms.gov/medicare/coverage/policies/2021/specialty/medicare-drug-price-negotiation-program).

support the development of medicines for patients with rare diseases. Daiichi Sankyo's comments are limited exclusively to that statement since CMS is refusing to consider comments on Section 30.

1. Orphan Drug Exclusion from Qualifying Single Source Drug

In the draft guidance, CMS states that it "is considering whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development."² As discussed in more detail below, the Inflation Reduction Act's (IRA) limits on the time that innovative drug manufacturers can recoup their research and development (R&D) investments incentivizes the development of medicines for large groups of patients and disincentivizes R&D focused on rare diseases. We believe there are actions within CMS' existing authority to implement the Program in a manner that continues to support and incentivize orphan drug development, and it is our sincere hope that CMS exercises this authority as expeditiously as possible for the benefit of patients.

In implementing this new law, a fundamental overhaul of the pricing and reimbursement of medications for Medicare beneficiaries, it is critically important to avoid unintended consequences that could have a negative impact on patients. This requires implementing the Program, consistent with CMS authority, in a manner that maintains a clear focus on patients and ensures not only short-term access to drugs that are already marketed, but also protects the R&D pipeline of new treatments and cures for patients who are the most vulnerable to shifting incentives.

a. Daiichi Sankyo's Commitment to Investing in Medicines for Patients with Unmet Needs

We appreciate CMS' interest and commitment to supporting the development of drugs for patients with rare diseases. Daiichi Sankyo shares this commitment to the R&D of new treatments and cures for patients with unmet needs and has invested in the development of drugs to treat rare diseases. At Daiichi Sankyo, passionate researchers are working every day using our science and technology to bring new medicines to patients who need them. Our dedication to transforming science into value for patients forms everything we do from our R&D strategy to product commercialization.

Our pipeline includes four medicines with orphan designations in clinical trials, reflecting our commitment to bringing new therapies to patients with unmet needs.³ These drugs are being studied with the goal of bringing effective therapies and improved quality of life to people with:

- Acute myeloid leukemia (AML) – a group of blood and bone marrow cancers, often spreading to the lymph nodes, liver, spleen, central nervous system, and testes. Only about 25% of patients with AML can expect to live 3 or more years, and 45% of patients with complete remission can expect similar prognosis.
- Netherton syndrome (NS) – a hereditary syndrome, characterized by skin inflammation and scaling, fragile hair, and being more prone to allergies, asthma, and eczemas. NS is very rare, with only 150 reported cases.
- Peripheral T-cell lymphoma (PTCL) – a very rare type of T-cell lymphoma that includes a diverse group of aggressive lymphomas, arising in the lymphoid tissues such as lymph nodes, spleen,

² Guidance at 11.

³ See Daiichi Sankyo, Our Pipeline, available at [Pipeline 3ADC \(daiichisankyo.com\)](https://www.daiichisankyo.com/pipeline).

gastrointestinal tract, and skin. Prognosis varies among subtype, but the most common type of PTCL is characterized as aggressive and has a poor prognosis.

- Pseudoxanthoma elasticum (PXE) –a hereditary disorder that causes some tissue in the body to become mineralized, resulting in symptoms that vary by person, but can include changes to the skin, to the retina of the eye that may result in significant loss of vision, to the cardiovascular system that may involve calcification of arteries and decreased blood flow, and to the gastrointestinal system that may result in bleeding in the stomach or intestines.

This research demonstrates the breadth of rare diseases, as well as the need to bring hope and improved outcomes to patients facing limited treatment options.

b. R&D Decisions Must Balance Science with Ability to Continue Pipeline Investments

Daiichi Sankyo’s researchers developing medicines for patients with rare diseases and other unmet medical needs must determine where to focus their work early in the development process. Our scientists must make the decision of whether to first evaluate a new chemical entity for a rare or for a non-rare population before testing even begins. Oftentimes, manufacturers may choose to first invest in researching a drug for a rare disease, which can involve smaller trials and may be able to show results earlier and come to market sooner than if tested first in a larger patient population. Because these studies typically include a small number of people, they can be used to provide evidence that a drug may be effective in later stages of development and help inform decisions about investing in larger, more costly trials. This benefits patients with rare diseases, who would then have access to new drugs sooner while the larger trials with more patients are still ongoing.

Those early decisions are led by the science, and the incentives established by the Orphan Drug Act and other congressional efforts have helped to provide companies like Daiichi Sankyo with the business case needed to put significant resources behind R&D for rare diseases. The IRA, however, provides a limited amount of time before a drug can be eligible for price setting. If Daiichi Sankyo and other innovative biopharmaceutical companies are not able to recoup those investments, or face a penalty for bringing a new therapy to a small group of patients as quickly as possible since there is a limited amount of time before a drug can be eligible for price setting, those R&D decisions will be reevaluated so that innovative companies are able to continue to invest in future therapies. This means that research into rare diseases could be curtailed significantly, if not slashed from portfolios entirely. It also means that the opportunity to learn more about a given molecule, and the rare disease itself, is lost along the way, even if a company does pursue its first indication in a bigger market. Even trials that eventually fail to show the benefit of a given therapy can add volumes of knowledge to the overall understanding of a disease, and that knowledge can serve as a steppingstone to other therapies that could be effective. Ultimately, the impact could be devastating to patients.

CMS’ guidance is aimed at the first initial price applicability year 2026, but it is impacting investment decisions right now. Since the passage of the IRA, innovative manufacturers have already made and continue to make decisions about which indications to invest in and how to sequence the launch of new products without clear guidance from CMS about how it plans to implement the orphan exclusion. How CMS implements this exclusion and when it provides that guidance will have immediate and long-term

impacts on people with rare diseases. Daiichi Sankyo urges CMS to provide that needed clarity expeditiously to guide its ongoing R&D analysis and provide companies with the opportunity to potentially unwind any decisions that may have already been made.

c. CMS Has the Legal Authority to Implement the Orphan Drug Exclusion to Support Orphan Drug Development

The IRA excludes certain orphan drugs from being eligible to be selected for price setting. Specifically, “the term ‘qualifying single source drug’ does not include ... [a] drug that is designated as a drug for only one rare disease or condition ... and for which the only approved indication (or indications) is for such disease or condition.”⁴ Consistent with the Guidance, if a drug or biological receives an additional indication outside the first orphan designation, it is no longer excluded from the definition of QSSD and is eligible to be a selected drug and subject to the Program’s price setting. The law requires that a drug is eligible for selection 7 years from approval, with the set price going into effect at 9 years. A biologic is eligible for selection at 11 years from licensure, with the set price going into effect at 13 years.

The statute requires that the timing for an orphan drug’s eligibility runs from the first approval outside the first orphan designation (*e.g.*, approval for a second disease or condition or receipt of a second orphan drug designation). That is when the orphan drug or biologic loses its exemption as a QSSD and becomes eligible for price setting. This interpretation is required to give full effect to the text of the orphan-drug exclusion, which prevents a drug from meeting the definition of QSSD, including its 7- and 11-year period provisions, if the conditions for the orphan exclusion are met.

d. Policy Reasons Compel CMS to Follow the Statute in Implementing the Orphan Drug Exclusion

In addition to the statute, policy reasons also compel CMS to implement the orphan drug exclusion this way. If the timing is retrospectively tied to the orphan drug's previously exempt approvals once the exemption is lost, then companies may be incentivized to wait or not seek orphan approval. Instead, they might conduct larger trials that take more time so that their first approval is for a larger population, and they can reach a larger number of patients in the 7- or 11-year period prior to being eligible for selection.

As described above, a company may be able to research a new drug or biologic for an orphan indication and bring it to market quickly, potentially bringing a curative therapy to a small set of patients with limited or no other treatment options. The manufacturer may also believe there are other promising indications that will take longer to research but would serve a much larger population of patients. If CMS interprets the 7- or 11-year clock to have already been running upon loss of the orphan exemption, this interpretation would incentivize the manufacturer to wait on the approval for the orphan indication, or not pursue it all, as it would “run the clock” on the 7/11 years on a very small population of patients.

However, if CMS reads the statute to tie eligibility for price setting to the date of the approval for a second disease or condition outside the orphan designation or receipt of a new designation, it preserves the incentive for a manufacturer to seek an orphan indication early and get the medicine out quickly to

⁴ Social Security Act § 1192(e)(3)(A).

an underserved group of patients. Specifically, it preserves the 7/11-year period for the subsequent indication for a larger group of patients. (See Appendix for illustrative example.)

Each of Daiichi Sankyo's orphan-designated drugs, while currently being tested for orphan diseases, has the potential to also address medical needs in broader, non-orphan patient populations. Because the IRA limits the time that biopharmaceutical companies can recoup their investments to 9 or 13 years before price setting, it pushes R&D toward development projects that enable a company to recoup its investment within a shorter period of time, since they cannot spread their costs over a longer period of time that includes a period of marketing only to a very small group of patients.

We cannot emphasize enough that companies like Daiichi Sankyo are making these R&D decisions now, and CMS cannot wait to act to provide companies like ours with needed guidance if it genuinely wants to "support orphan drug development." We urge CMS to provide innovative pharmaceutical companies with the clarity needed to know that our investments in rare disease drugs will continue to be viable and that patients with rare diseases will continue to benefit from robust pipelines offering new treatments and cures.

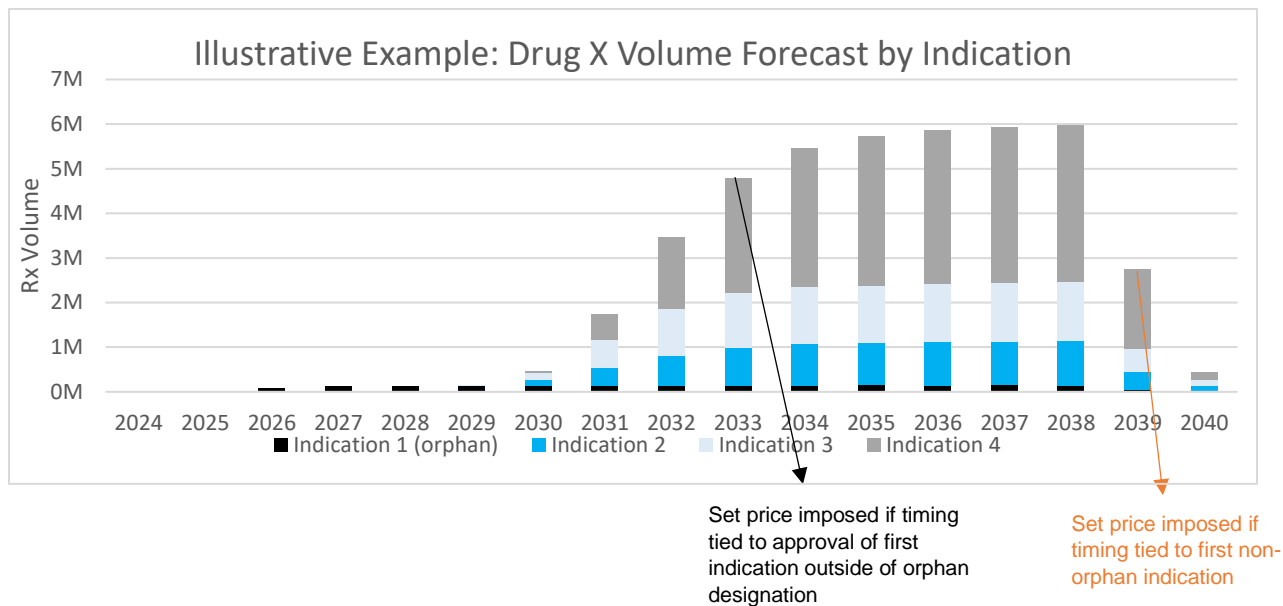
Daiichi Sankyo thanks CMS for its consideration of these comments responding to CMS' interest in additional actions to support the development of orphan drugs. We look forward to working with CMS on our shared goal of addressing the unmet needs of patients with rare diseases. If you have any questions or would like additional information on Daiichi Sankyo's experience in the development of orphan-designated drugs, please contact me at apezalla@dsi.com.

Sincerely,

/s/

Amanda Pezalla
Assistant General Counsel, Head of Government Affairs and Public Policy
Daiichi Sankyo, Inc.

Appendix





April 13, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Day One Biopharmaceuticals appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance). While we recognize that CMS is not accepting comments to section 30, we hope you will consider our comment given the potential impact section 30 could have on patients and biotechnology companies that are innovating in critical areas of unmet need.

Day One is unlike most other biotechnology companies: our focus is on pediatric oncology drug development. Pediatric oncology is an area of critical unmet need that is typically an afterthought in the pharmaceutical industry. Our lead product candidate, tovorafenib, is a small molecule type II pan-RAF kinase inhibitor currently under evaluation in a pivotal Phase 2 clinical trial among pediatric, adolescent, and young adult patients with relapsed or progressive pediatric Low-Grade Glioma (pLGG). The product has been granted Breakthrough Therapy and Rare Pediatric Disease designations by the U.S. Food and Drug Administration (FDA), as well as Orphan Drug designation from the FDA and the European Commission (EC).

We are concerned that the Drug Price Negotiation Program's exclusion for certain orphan drugs is overly restrictive and could harm products like tovorafenib. We recognize that the statute itself limits the exclusion to "[a] drug that is designated as a drug for only *one* rare disease or condition under section 526 of the Federal Food, Drug, and Cosmetic Act and for which the only approved indication (or indications) is for such disease or condition." SSA § 1192(e)(3)(A). Although CMS has reaffirmed this definition in section 30.1.1, it has also stated that it "is considering whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development." To achieve this objective, we encourage CMS to take broad actions that continue to incentivize the development of orphan drugs. For example, CMS can develop a policy to grant maximum fair prices at the statutory ceiling to any selected drug that only has indications for rare diseases. Additionally, CMS could exercise its discretion when selecting drugs to delay the entry of certain orphan drugs that do not meet the criteria for the exclusion.

CMS should take particular care to incentivize the development of small molecule orphan drugs. Currently, the Drug Price Negotiation Program and its implementation details in section 30 directly threaten the ability of companies like Day One with small molecule drugs in development to build sustainable businesses and bring novel therapeutic



options to children with cancer and other rare diseases. Without reasonable incentives to invest in small molecule drugs and pursue rapid registration paths for rare and neglected patient populations, it becomes extremely difficult for companies like ours to stay in business and continue to develop new medicines for these patients. This legislation will flip the model upon which the biotech industry has been built and will not only impact innovation, but worse, severely limit access to cutting-edge treatments.

Until Day One was founded a few years back, no other companies were taking a chance in pediatric oncology drug development. This lack of investment was due, in part, to the small patient populations covered. Through our drug development efforts, we are changing the paradigm and bringing hope to the pediatric cancer community – academics, patients and their families, and patient organizations, who have all been overlooked when it comes to therapeutic innovation. Unless CMS acts, the Drug Price Negotiation Program will upend all of this work and relegate children with cancer to the back of the innovation line once more.

On behalf of the children living with cancer, and the scientists and oncology community that support them, I ask that you please work with Congress to move the timing for NDA-path negotiations from 9 years to 13 years, the same time period as BLA-path drugs. This would ensure that the Drug Price Negotiation Program does not negatively impact the market for pediatric oncology orphan drugs.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to rare disease patients is minimized. Please contact me at Jeremy.bender@dayonebio.com if you have any questions regarding our comments.

Jeremy Bender, Ph.D.
Chief Executive Officer
Day One Biopharmaceuticals

A handwritten signature in blue ink, appearing to read "Jeremy Bender", with a long, sweeping horizontal line extending to the right.



April 14, 2023

The Honorable Chiquita Brooks-LaSure, Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building, Room 445-G
200 Independence Avenue, SW
Washington, D.C. 20201
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Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

We appreciate the opportunity to provide comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (“CMS”) website on March 15, 2023 (the “Memorandum”). We look forward to continued discussions with CMS.

There is a burgeoning health crisis in America due to the lack of treatments for diseases suffered by our seniors. Last summer, the U.S. Congress convened a roundtable of experts from government, academia, and industry to discuss its severity.¹ Alzheimer’s Disease has been identified as the fifth leading cause of death among adults over 65 years, and it alone will cost Americans over \$1 trillion dollars a year by 2050.² One disease is driving an immense burden on society. What society needs most now is research into the underlying biology of neurodegeneration so that we can discover a cure. This is our mission at Denali Therapeutics.

Denali Therapeutics Inc. (“Denali”) is a biopharmaceutical company founded with the mission to defeat degeneration by developing a broad portfolio of potential medicines engineered to cross the blood-brain barrier (BBB) for the treatment of neurodegenerative and lysosomal storage diseases, including Alzheimer’s, Parkinson’s, ALS, and rare neurodegenerative diseases. We believe that by rigorously assessing genetically validated targets, engineering delivery across the BBB, and guiding development through biomarkers, that we can improve our chances of finding a cure. Since our founding in May 2015, our team has built a pipeline that includes 7 clinical development programs, including 4 late-stage clinical studies, published over 20 papers in top-tier scientific journals and been awarded over 150 patents worldwide. Denali is based in South San Francisco, California, and employs over 400 individuals, many of whom are personally impacted by the diseases we seek to treat.³

¹ The Economic Cost of Alzheimer’s Disease: Hearing Before the Joint Economic Committee, 117 Cong. (2022), available at <https://www.jec.senate.gov/public/index.cfm/democrats/issue-briefs?id=02F4CADC-954F-4E3B-8409-A4213E3C0759> (last accessed April 13, 2023).

² Wong, W., Economic burden of Alzheimer disease and managed care considerations, *Am. J. Manag. Care*, 2020 Aug;26(8 Suppl):S177-S183.

³ For additional information, please visit www.denalitherapeutics.com.

Denali strongly believes in ensuring patients have access to medicines they need today and, in the future, and is concerned that the Guidelines will inadvertently impede this access. CMS's goal to lower the cost of prescription drugs for seniors and people with disabilities is commendable, and Denali supports Medicare price negotiations that are fair and consistent. Our comments focus on the potential unintended harms from the most drastic changes proposed in the negotiation process. We suggest alternatives that we believe will better achieve our shared goal of encouraging innovation and managing the costs of medicines.

- The negotiation process could result in eroding incentives for biosimilar development from drastic price cuts when biosimilars will be launching competing alternatives.
- The negotiation procedures should not preclude our ability to choose the optimal modality for a given therapeutic approach. By favoring biologics over small molecules, the negotiation process could create perverse incentives that could ultimately limit new treatment options for patients.
- The negotiation process should encourage new and post-approval research and development in medicines for high unmet needs by fixing the orphan drug exclusion and including the full post-approval costs of research and development in the MFP calculations.

I. Denali Respectfully Requests CMS to Consider Comments on Section 30 of the Guidelines

Denali recognizes that CMS is not requesting comments on Section 30 of the Memorandum.⁴ However, given the significant and substantive impact of the final rules, Denali would have provided these comments to CMS if it had been given the opportunity.

II. The Earliest Timing of Selection of for All Medicines Should be 11 Years from Approval to Avoid Non-Medical Based Development Decisions

We encourage CMS to adopt a uniform, 11-year earliest selection timeline for all small- and large-molecule treatments, or in the alternative, lessen the impacts on small molecule drugs through the MFP negotiation process. In Section 30.1 of the Memorandum, CMS has stated that it intends to distinguish between medicines based on their approval pathways, i.e., NDA- vs. BLA-approved medicines. We note that there is no scientific or medical rationale for such a distinction. Furthermore, in addition to being arbitrary, this distinction risks creating negative incentives for developing NDA-approved medicines (i.e., small molecule medicines) that are badly needed for diseases of the brain that affect seniors. Small molecule treatments may freely penetrate

⁴ Denali respectfully requests that CMS reconsider its decision to issue final rules related to Section 30 of the Guidelines. Notice and comment procedures are required under the Administrative Procedures Act. See 5 U.S.C. § 553(b) (2023). CMS may evade this APA obligation only "in emergency situations, or where delay could result in serious harm." *Jifry v. FAA*, 370 F.3d 1174, 1179 (D.C. Cir. 2004). The Memorandum falls short of the high threshold needed to invoke the emergency situations exception. Instead, the Memorandum claims that CMS may issue final rules without the notice and comment procedures because of the "complexity of the preparation that must be undertaken in advance of the publication of the selected drug list by September 1, 2023." Memorandum at 2. This is insufficient. In fact, the D.C. District Court already has rejected complexity as a basis for good cause. See *Nat'l Venture Capital Assoc. v. Duke*, 291 F.Supp.3d 5, 18 (D.D.C. 2017) (rejecting complexity as a basis for good cause). CMS will have had more than a year since the IRA was enacted to promulgate rules before September 1, 2023. Good cause "cannot arise as a result of the agency's own delay." *Wash. All. of Tech. Workers v. U.S. Dep't of Homeland Sec.*, 202 F.Supp.3d 20, 26 (D.D.C. 2016), *aff'd*, 857 F.3d 907 (D.C. Cir. 2017). The reasons for avoiding notice and comment procedures in the Memorandum could expose CMS to prolonged litigation and uncertainty surrounding implementation of the IRA. Denali urges CMS to reconsider.

cells (important for therapeutic targets that are present only inside cells), can be manufactured cheaply, and can be given to patients orally. Disincentivizing small molecule program investment risks depriving patients of what might be the only or best treatment for their disease.

Eleven years is an appropriate timeframe for selection into the negotiation program. Although it would result in less than the typical 14 years of exclusivity generally afforded under U.S. patent protection, it would create a level playing field for therapeutics and would focus development decisions on the likelihood of a drug's success at treating a disease, rather than an arbitrary factor like its approval pathway.

III. The Orphan Drug Exclusion Could Create Disincentives for Post-Approval Development, Hurt Patient Access, and Increase Unproven Off-Label Use

CMS should not subject orphan drugs to the negotiation process after they are developed in additional indications. CMS proposes to limit the orphan drug exclusion to medicines that are only approved for one rare disease. This would discourage the development of the medicine in other indications, in order to avoid subjecting the product franchise to price negotiations. For example, a particular medicine may first be developed for amyotrophic lateral sclerosis (ALS), an orphan indication. Post-approval development of the medicine in other rare neurological indications, such as leukodystrophies, could be disincentivized under the rules because approval in the second indication subjects the entire product franchise to the negotiation process. Manufacturers will also be incentivized to make different decisions on sequencing indications and determining global launches, which could lead to reduced patient access to drugs that could potentially treat their disease.

Furthermore, any impediments to post-approval drug development of orphan drugs could lead to increased off-label use. Previous studies have demonstrated that off-label use of approved medicines can be very high, and that most off-label uses have little or no scientific basis.⁵ In other words, a substantial share of prescribing is not validated by FDA-regulated studies and is based on weak or no data.⁶ This type of off-label prescribing should not be encouraged. If manufacturers were incentivized to do post-approval development into a broad range of indications, then FDA-regulated data would become available to better guide physician prescribing and could reduce off-label use. Therefore, investment into FDA-regulated development of products covered by the orphan drug exclusion should be encouraged under CMS's Guidance. Regulated and expanded indications are good for patient safety and access and should not be punished.

The negative incentives discussed above could be mitigated by not subjecting drugs to the negotiation process after they are developed in additional indications. Alternatively, creating a level playing field for all medicines that includes selection at the earliest 11 years from approval, regardless of approval pathway, would help alleviate the concerns.

IV. MFP Calculations Should Consider the Full Research and Development Costs of a Medicine to Incentivize Rigorous Research and Development

Denali is concerned that the Guidelines' proposed limitations on recovery of costs do not consider the full cost of drug development. Section 50.1 of the Guidelines provides that a drug's maximum fair price ("MFP") would consider research and development costs of the Primary manufacturer for the selected drug, and the

⁵ Radley D.C., *et al.*, Off-label prescribing among office-based physicians, *Arch. Intern. Med.*, 2006;166(9):1021–6.

⁶ Sahragardjoonegani, B., *et al.*, Repurposing existing drugs for new uses: a cohort study of the frequency of FDA-granted new indication exclusivities since 1997, *J. Pharm. Policy Pract.*, 2021;14:3

extent to which the Primary Manufacturer has recouped those costs. As defined in the Guidelines, “Research and Development Costs” would explicitly exclude “costs associated with *ongoing* basic pre-clinical research, clinical trials, and pending approvals” (emphasis in original).⁷

Denali notes that the definition excludes important costs that should be included for negotiating the MFP. For example, the basic pre-clinical research period is defined in the Guidelines as beginning on the date of initial discovery of the drug, or when the rights to hold the NDA/BLA were acquired.⁸ However, this definition has the potential to exclude important costs into potential drugs in the same class that did not ultimately become the drug subject to the IND filing. This limitation in the definition could set up incentives to limit research in similar potential candidates, thus limiting the overall knowledge of the potential safety and therapeutic potential of the mechanism of action and the drug that is ultimately approved. Costs should include research and development costs of failed trials that did not lead to FDA-approved indications and should include ongoing safety and efficacy research costs post-approval.

The definition of abandoned and failed drug costs are defined, but the full value of the costs of research and development of drugs with the same mechanism of action should be included. For example, if the approved drug is the second such compound studied in the class, the costs should include the studies of the first compound even though the drug was not advanced, given that it contributed to the learning and development of the drug that ultimately became subject of the approved NDA or BLA.

The Congressional Budget Office recently issued a report that contained findings that state manufacturers make high levels of investment into drugs that don't make it to the NDA or BLA stage for a variety of reasons, but nonetheless contribute to the success of the approved drug product:

In recent studies, estimates of the average R&D cost per new drug range from less than \$1 billion to more than \$2 billion per drug. Those estimates include the costs of both laboratory research and clinical trials of successful new drugs as well as expenditures on drugs that do not make it past the laboratory-development stage, that enter clinical trials but fail in those trials or are withdrawn by the drugmaker for business reasons, or that are not approved by the FDA. Those estimates also include the company's capital costs—the value of other forgone investments—incurred during the R&D process. *Such costs can make up a substantial share of the average total cost of developing a new drug. The development process often takes a decade or more, and during that time the company does not receive a financial return on its investment in developing that drug.*⁹ (emphasis added)

The Guidance should reflect the reality and necessity of these investments that are broader than the one molecular entity that is subject to the NDA or BLA in order to incentivize the most rigorous research possible.

V. Drug Price Negotiations Should Not Undercut Healthy Competition from Generics and Biosimilars that Controls Drug Costs

The Guidance should create better incentives for healthy competition in the marketplace. Denali believes that strong patent and exclusive marketing rights, followed by healthy generic and biosimilar

⁷ Memorandum at 82.

⁸ Memorandum at 83.

⁹ Research and Development in the Pharmaceutical Industry, Congressional Budget Office, April 2021, available at <https://www.cbo.gov/publication/57025> (last accessed April 12, 2023).

competition at the end of exclusivity periods, are the best way to encourage the continued discovery and development of medicines for high unmet needs of patients. In fact, the generic and biosimilar market in the U.S. represents a healthy control on drug prices. From 2021-2025, it has been estimated that biosimilar medicines will have reduced drug spending in the U.S. by \$38 billion dollars and could be as high as \$124 billion dollars.¹⁰ To maximize these savings, companies need incentives to develop biosimilars. A typical biosimilar company will invest between \$100-300 million dollars over 10 years to launch a biosimilar medicine.¹¹ Companies are only willing to take that risk if there is a potential for profit after approval. Yet, the biosimilars industry sees the IRA as eliminating incentives. According to one biosimilar leader, under the IRA, the U.S. market could “see the price of the brand biologic cut by 60% by the Department of Health and Human Services. That would eliminate some, if not most, of the investment made by developers to make more affordable medicines available to patients. Given the uncertainty around what drugs the government could decide are subject to price negotiation, biosimilar development could be forestalled for dozens of medicines. The overall effect would be more branded drugs maintaining their monopolies for longer.”¹²

Denali appreciates the opportunity to provide comments on the Guidelines and CMS’s consideration of our comments as the Drug Price Negotiation Program policies are developed. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and successfully, in a way that incentivizes research and development into medicines for high unmet medical needs and improves patient access to medicines. Please feel free to contact one of us if you have any questions regarding our comments.

Respectfully Yours,

Denali Therapeutics Inc.



Katie Peng
Chief Commercial Officer



Christopher Walsh
General Counsel

¹⁰ Mulcahy, A. & Buttorff, C., Projected US Savings From Biosimilars, 2021-2025, Am. J. of Manag. Care, 2022, 28(7):329-335.

¹¹ Blackstone, E., *et al.*, The Economics of Biosimilars, Am. Health Drug Benefits, 2013 Sep-Oct; 6(8):469-478; Fontanillo, M., *et al.*, Three imperatives for R&D in biosimilars, McKinsey & Company, August 2022, available at <https://www.mckinsey.com/industries/life-sciences/our-insights/three-imperatives-for-r-and-d-in-biosimilars#/> (last accessed April 13, 2023).

¹² Leonard, D., The hurried push by Congress to address drug costs shouldn’t undermine the vast savings from generics and biosimilars, STAT News, Nov. 6, 2021, available at <https://www.statnews.com/2021/11/06/hurried-bills-congress-shouldnt-undermine-vast-savings-generic-biosimilar-drugs/> (last accessed April 13, 2023).



April 13, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Design Therapeutics appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

Design Therapeutics is pioneering the field of small molecule genomic medicine, which holds the potential to safely and effectively deliver meaningful benefit to patients suffering with serious genetic disorders. Our novel small molecule therapeutic candidates called gene targeted chimera or GeneTAC™ molecules target the underlying cause of inherited genetic diseases. Through our proprietary GeneTAC™ platform, we can design and develop therapeutic candidates that dial gene expression up or down without requiring gene editing.

The development of drugs to treat genetic disease had been focused on novel complex modalities such as gene therapy, gene editing, and antibodies, which are large biologics. But through our GeneTAC™ platform, we have shown the ability to effectively target and modulate expression of specific mutated genes that cause serious disease. Our lead compound for the treatment of Friedreich ataxia (FA), a rare inherited, degenerative disorder that leads to permanent disability and shortening of life span, entered the clinic in 2022. Initial findings from our Phase 1 clinical trial in people suffering with FA indicate that our FA GeneTAC™ molecule could indeed restore transcription of the mutated frataxin gene, thus providing proof of mechanism for this novel modality. We plan to bring our second GeneTAC™ development candidate into the clinic to treat Fuchs endothelial corneal dystrophy (FECD), an inherited genetic disorder that leads to degeneration of the cornea and vision impairment in approximately 4% of people over 40 years of age. Currently, therapeutic options for FECD rely on corneal surgery for individuals with more advanced disease, leaving the majority of patients without treatment for years, sometimes decades. The FECD GeneTAC™ small molecule now under development for topical ocular delivery (eye drops) has been shown in *in vitro* studies to block transcription of the mutant gene, the root cause of the disease, potentially slowing or reversing visual impairment.

GeneTAC™ small molecules are able to overcome major limitations found in large biologic medicines, such as delivery into the brain and heart (relevant for treating FA) and the cornea (relevant for FECD), and can be formulated for different routes of administration, and optimized through medicinal chemistry toward favorable pharmaceutical properties. Like other small molecules, GeneTAC™ molecules can be tailored to a desired effect and tolerability, and do not result in irreversible genetic modifications (e.g., from gene editing and gene therapy).

We believe there is vital importance to continue and foster deployment of R&D resources and investment toward developing novel small molecule genomic medicines and afford protections and commercial exclusivity at similar levels afforded to that proposed in the IRA for biologics products.

The following are comments on specific provisions in the IRA which we believe will directly impact the development of potentially transformative novel small molecule genomic medicines toward a successful NDA and commercialization.

- I. **Provision (30.1):** Medicare negotiation for NDA-path drugs at only nine-years post-launch significantly disadvantages small molecules like the ones we are developing when compared with biologics and makes it more difficult for us to raise the capital necessary to fund their development. We urge you to work toward creating parity between small molecules and biologics by allowing small molecules the same 13-year exclusivity window as biologics. Progress in diseases like FA and FECD (not to mention Alzheimer's, heart disease, many cancers, etc.) relies on our and others' ability to attract funding for small molecule drug candidates. The current distinction could skew investment toward biologic drug development, complex modalities like cell and gene therapy, and away from diseases that have comparable healthy impact on Medicare populations.
- II. **Provision (30.1.1):** To be considered for the orphan drug exclusion, the drug or biological product must (1) be designated as a drug for **only one rare disease or condition under section 526 of the FD&C Act** and (2) be approved by the FDA only for one or more indications within such designated rare disease or condition. This may limit our ability to explore additional uses for drugs that could help multiple orphan diseases like FA because they would no longer qualify for an exemption from price negotiation under the IRA. This prevents companies from trying to treat multiple orphan diseases with drugs that have already overcome a narrow funnel of early development, avoiding duplication of development costs and development risks, and hampers orphan drug development. With recent scientific breakthroughs (e.g., including potentially transformative novel drugs being developed at Design Therapeutics), small molecules are just as promising for treating serious diseases and therefore should receive the same considerations by CMS.
- III. **Provision (50.2):** Cost-effectiveness math embraced by ICER in the US and other HTA bodies elsewhere (e.g., NICE in the UK) is so simplified that it excludes many demonstrable benefits of medicines resulting in extreme underestimations of the value of new medicines. This math can then serve as an excuse for plans to refuse coverage, telling patients that the medicines aren't worth their prices instead of admitting that the plan just doesn't want to pay. Specifically, direct, and indirect costs as a result of an FA or FECD diagnosis exceeds costs circumscribed to select symptoms used for value calculations by CEAs. For example, FA is a progressive, disabling disorder that limits mobility starting in the second decade of life, and eventually requires the use of wheelchairs and other assistive devices. A therapeutic intervention that targets the cause of the disease, such as the one being developed by Design, has the potential to slow disease progression, reverse some symptoms and, if deployed early, prevent development of symptoms. A novel, transformative therapeutic like this could not only reduce disease symptoms and patient burden, but also substantially reduce need for caregiver services (be it from family or professional), allow a person with FA to complete their education and obtain/keep a job, etc. Further, a more effective treatment of FA could reduce costs associated with increased healthcare utilization (to manage a myriad of disease complications), loss of productivity due to the need for a caregiver, household accommodation to adapt to

disabilities, etc. In the case of FECD, progressive visual impairment can limit daily activities for years before patients are eligible for a surgical intervention (currently the only available treatment), which has its own risks and costs. Visual impairment affects mobility, ability to work, live independently, etc; each of which adds not only to direct patient suffering but also substantial costs to mitigate limitations imposed by visual impairment.

Instead of assessing overall costs associated with a particular disease, thus better assessing the true potential overall value of a novel, more effective therapeutic, ICER-like CEA utilizes assessments with over-simplified math that undervalues certain groundbreaking drugs. Considering that novel drugs will eventually go generic (e.g., many psychiatric and neurological drugs, most antibiotics, cardiovascular medicines, etc.) and will continue to keep us out of hospitals and nursing homes, costs of which do not “go generic”, ICER-like CEA talks society out of paying a finite mortgage for a drug even though the alternative is paying a rising rent forever. Undervaluing potentially transformative new drugs would signal to investors that the value of new medicines will be willfully underestimated and that their development will not be rewarded, which will turn investors away from funding biomedical R&D, locking us into today’s standard of care and the rising cost of hospitals and nursing homes.

- IV. **Provision (40.2.2):** CMS prohibitions on data disclosure and destruction of related documents make it impossible for companies to understand which value components CMS measures to determine MFP. Transparency is important so we can understand how CMS considers what is a “fair price.” We also worry that if CMS were to impose this kind of restriction, we would be unable to inform our board and the investor community about the negotiation process so they can make informed decisions about the future of drug development.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact me by telephone at (858) 692-5081 or by e-mail at jsiffert@designtx.com if you have any questions regarding our comments.

Sincerely,

A handwritten signature in black ink, appearing to read 'Joao Siffert', with a stylized, fluid script.

Joao Siffert, MD
President and Chief Executive Officer
Design Therapeutics

jsiffert@designtx.com

VIA ELECTRONIC SUBMISSION

The Honorable Chiquita Brooks-LaSure
Centers for Medicare and Medicaid Services Administrator
200 Independence Avenue, S.W.
Washington, D.C. 20201

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Brooks-LaSure:

We are writing to comment on the initial guidance, entitled: “Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments” (Guidance), published on March 15, 2023, by the Centers for Medicare and Medicaid Services (CMS). The Guidance addresses the implementation of sections 11001 and 11002 of the Inflation Reduction Act (IRA), which establishes the Medicare Drug Price Negotiation Program (Negotiation Program) to negotiate maximum fair prices (MFPs) for certain high-expenditure, single-source drugs and biologics. The Guidance provides further detail about CMS’s intended implementation of the Negotiation Program and solicits stakeholder feedback on specific issues surrounding this program, including the negotiation factors, how CMS will determine its pricing offer to a drug manufacturer, the negotiations process, and others.

While Congress exempted the IRA’s implementation from a requirement for a formal notice-and-comment rulemaking process, CMS has described in the Guidance a process for timely public input on how the MFP for a drug will be determined. We appreciate CMS’s efforts to solicit comments on most aspects of the Guidance pertaining to the implementation of the Negotiation Program, which has a tight statutory timeline for initial application in 2026.

The Robert J. Margolis, MD Center for Health Policy at Duke University (the Duke-Margolis Center or the Center) generates and analyzes evidence across the spectrum of health policy with the goal of improving health care, health, and health equity while avoiding unnecessary costs. A core mission of the Center is to focus on increasing the value of biomedical innovation to patients. As part of these efforts, we study the design, implementation, and feasibility of value-based payment (VBP) arrangements for medical technologies, which shift away from payments based on volume and promote payments based on the impact of the treatment. These approaches include payments linked to better evidence and outcomes, and “subscription” or population-based payments, for biomedical technologies, complementary to shifts in payments to health care providers that are similarly linked to improving outcomes and decreasing total medical expenditures. The suggestions below are informed by the Center’s experience and research in developing approaches to payment reform that support better evidence and outcomes for patients and better value across the system; in analyzing the impact of the current legal and regulatory environment on their adoption; and in working with multiple stakeholders to address the operational

challenges to their use. They are also informed by the collaborative work of the Center's Value for Medical Products Consortium (the Consortium), and by the work of the Center's Real-World Evidence (RWE) Collaborative, but may not represent the opinions of every member of these collaborations. Our Consortium and/or RWE Collaborative members are in many cases providing their own comments on behalf of their organizations.

Our comments reflect Duke-Margolis's independent analyses of the Guidance and recent work undertaken by the Consortium and the Collaborative. Our recommendations describe opportunities for CMS to refine the Guidance in light of considerations related to RWE and the use of quality evidence, program integrity and transparency, and arrangements that align drug payments with their observed value. An overarching theme in our comments is the importance of implementing the Negotiation Program in a sustainable way for years to come despite the substantial requirements with limited time statutorily imposed on CMS. To this end, we suggest that CMS lay out a clear *initial* framework for how it intends to carry out MFP determinations while also describing a pathway for refinements over time as experience with the program grows beyond Price Applicability Year 2026. Specifically, our recommendations are for CMS to:

1. Implement a clear framework for assessing comparative effectiveness and translating such analyses to prices
2. As part of this framework, describe how real-world evidence development, including evidence related to additional indications, will impact CMS's MFP determinations
3. Develop mechanisms to facilitate alternative payment arrangements for drugs that accomplish the intended goals of the IRA
4. Clarify how the manufacturer-specific factors will be used to guide the MFP, and collaborate to support accurate and efficient data collection
5. Clarify additional considerations for implementing the Negotiation Program

Our detailed comments are as follows:

Implement a clear framework for assessing comparative effectiveness and translating such analyses to prices

As described in the Guidance, CMS intends to consider evidence about therapeutic alternatives for a drug selected for price negotiation through an evaluation of the body of clinical evidence by considering factors in two areas: outcomes and safety. This evidence review will be informed by evidence submitted by members of the public, including drug manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested parties. CMS also intends to conduct its own literature review as part of this evidence review, prioritizing research that is methodologically rigorous. CMS intends to consider research on, and RWE relating to, Medicare populations as particularly significant to its assessment. CMS will place significant weight on assessing whether the drug fills an unmet medical need, which CMS defines as treating a disease or condition in cases where very limited or no other treatment options exist. CMS will then use this assessment of comparative effectiveness to adjust the initial price it set for the drug, which will generally be the net price of the closest therapeutic alternative in Medicare. CMS

should clarify its methodology for setting the initial price in case there are multiple therapeutic alternatives (for example, via some type of weighted average).

The Guidance provides a thoughtful overview of how it will consider evidence about therapeutic alternatives and the evidence assessment's impact on the determination of the negotiated price. The final guidance should build on stakeholder comments, including ours, to provide a more detailed framework that encompasses the major comparative effectiveness considerations, including how evidence and stakeholder engagements would contribute to the overall evidence assessments concerning the drug and its alternative treatment(s). CMS proposes a very broad and flexible "qualitative" approach which involves *"adjusting the starting point upward or downward relative to the clinical benefit offered by the selected drug compared to its therapeutic alternatives."* The agency also suggests that it wants to retain broad discretion regarding the evidence it will consider for setting the MFP, stating that it intends to consider a range of evidence types pertaining to the selected drug's therapeutic alternatives from a range of stakeholders, including evidence submitted by the public and patient-reported data, giving itself substantial flexibility to consider evidence from a variety of sources.

Such flexibility and broad discretion are understandable, especially for a new program facing a complexity of factors under a tight implementation deadline. However, flexibility also means uncertainty about how different types of evidence and contributions will matter (or not) in the assessment and the final MFP determination. Uncertainty will result in less effective investment and less investment in developing evidence that could improve the understanding of a drug's comparative effectiveness and thus its impact and use in Medicare beneficiaries. To encourage investment in drugs and supporting evidence that matter for Medicare beneficiaries, CMS should develop a plan for implementing an increasingly clear and rich framework for how different kinds of comparative effectiveness assessments will be integrated. Along with transparency about how it applies this qualitative framework to assessments over time, the assessment framework will become clearer and more robust with additional experience, potentially encouraging more drug development and supporting evidence development in ways that demonstrably improve outcomes and safety for Medicare beneficiaries.

To start this process, CMS should do more now to describe an initial guiding qualitative framework that will clarify the dimensions of comparative effectiveness that it will consider, how it will weigh different kinds of potentially relevant evidence (including RWE), and what evidence would lead to upward or downward price adjustments (including whether additional product improvements or indications could lead to upward adjustments, as we discuss further below).

As the IRA gave CMS considerable flexibility in how to incorporate comments and experience in the implementation of the price negotiation, CMS could describe the most important aspects of its comparative effectiveness assessments that should be detailed now and what aspects will require additional time and experience with the Negotiation Program implementation to help achieve better clarity. This more explicit Negotiation Program framework should describe how CMS intends to treat various evidence types in this process and lay out a framework for how the agency will engage with, and consider evidence from, different types of publicly reported studies and other submissions from stakeholders to support predictable, reliable assessments of comparative effectiveness.

For example, according to the Guidance, the use of RWE in its comparative effectiveness assessments may include evidence generated from patient-reported outcomes (PRO) data. In fact, value assessments that can systematically describe real-world value through PROs derived from electronic medical records or other RWE sources can address uncertainty around the real-world value of any drug under comparison,¹ but meaningful PRO studies can be costly to implement reliably. CMS could begin by describing PRO evidence likely to be most relevant to assessments in therapeutic areas that will be included in early negotiations, solicit further comments (and rely on existing tools and examples to incorporate PRO data) to help clarify how it will consider such evidence, and then provide transparent summaries of how such evidence contributed to the early assessments. Over time, this process would provide an increasingly clear and rich framework on how PRO-related evidence impacts CMS's qualitative assessments, which will drive more effective investment in relevant studies that include PROs.

CMS could create an initial “dashboard,” and refine it over time, to track and characterize key potential dimensions of the drug's impact on outcomes and safety that influence its assessments. Such a dashboard should focus on dimensions that matter to beneficiaries and improving health equity, goals that align with CMS strategic priorities and measures across its Medicare payment programs. This would help improve clarity about the basis for MFP determinations, and help guide input from beneficiary, consumer groups, and other stakeholders, to help CMS achieve its stated goals for the program. Below we provide additional suggestions for the use of such dashboard by CMS in the context of the other factors that it will consider in setting the MFP, as well as tracking the potential broader impacts that the Negotiation Program could have on drug access and innovation.

In developing its initial qualitative framework for comparative effectiveness and associated key metrics, CMS can draw on experience in the United States and elsewhere to describe how its comparative effectiveness assessments will inform a drug's price relative to its comparator. Several countries, such as France and Germany, use qualitative frameworks to integrate evidence on the comparative benefits and risks of alternative treatments in their drug price negotiations. These countries use scoring systems that rate the level of the “added benefit” the drug in question provides over a comparator product, and each level is typically tied to a range of payment adjustments. Some private payers use similar approaches.

This qualitative framework can also provide increasingly clear guidance on how CMS will consider the strength of evidence for the added health benefit, as described above, by prioritizing methodologically rigorous research. For example, the Institute of Clinical and Economic Review (ICER) assigns a level of certainty to its evidence finding, combining the magnitude of the comparative benefit with the level of certainty in the existing body of evidence for a drug. (In contrast to CMS's stated goal, Germany's framework appears to place most weight on more traditional randomized clinical trials, not other types of RWE; we support CMS's emphasis on RWE especially since its framework will be applied years after a product reaches the market.) Here, CMS could describe the kinds of evidence (and strength) likely to achieve the statutory ceiling price for a drug that presents a substantial clinical benefit compared to its

¹ Wu AW, Kharrazi H, Boulware LE, Snyder CF. Measure once, cut twice--adding patient-reported outcome measures to the electronic health record for comparative effectiveness research. *J Clin Epidemiol.* 2013 Aug;66(8 Suppl):S12-20. doi: 10.1016/j.jclinepi.2013.04.005. PMID: 23849145; PMCID: PMC3779680.

alternative treatment(s) in a relevant therapeutic area, while creating various payment “tiers” below the statutory ceiling for drugs demonstrating various levels of evidence short of a major improvement.

Similarly, CMS could describe the kinds of limited differences in meaningful outcomes and safety that would not support additional payment compared to a less expensive treatment. The comparative effectiveness methods CMS will use should provide increasingly clear illustrations of how to integrate differential impacts in the different dimensions of outcomes that may matter to patients, and how much any given difference in outcomes that matter would increase or decrease a selected drug’s “price category” from the price of its therapeutic alternative.

In addition to a pathway to an increasingly detailed qualitative framework, and a growing set of summary reports on implemented cases of price negotiation, CMS could provide more clarity to involved manufacturers through regular opportunities for manufacturers to consult early with CMS – beginning soon after a potentially relevant product comes to market and perhaps even before, in the pivotal trial design and implementation stage. CMS should also consider opportunities for input from a broad range of stakeholders to help flesh out its framework in particular relevant therapeutic areas. Especially in the early stages of Medicare price negotiation, these steps will help reduce uncertainty and generate the evidence and drug investments aligned with CMS broad goals. Food and Drug Administration (FDA) programs that provide regular and predictable meetings and public engagement opportunities have been very helpful for supporting investments by product developers in efficient and effective evidence development for products to demonstrate whether they meet FDA safety and effectiveness standards. Such programs could be similarly helpful here.

We note that, because these comparative effectiveness systems do not assess the evidence on benefits relative to costs, they will not clearly and easily reduce to a single-dimensional measure like cost-effectiveness. CMS comparative effectiveness methods must therefore consider how to integrate differential impacts in the multiple dimensions of outcomes that may matter to patients, and how much any given improvement in outcomes that matter should impact price. To augment its qualitative analyses, CMS could describe how particular quantitative assessment methodologies (other than quality-adjusted life years, or QALYs) could inform its qualitative framework. Potentially useful quantitative comparative effectiveness metrics such as equal value life years (evLY) have been developed to address concerns of potential discrimination from the use of QALYs.

Finally, price differences may well be anchored to quite different pricing or value levels across different therapeutic classes, even if CMS describes a clear and consistent basis for assessing an MFP relative to a reference product across different therapeutic areas. CMS should monitor whether such differences emerge, and develop ways to address them over time. This makes it even more important for CMS to continue to work toward transparent and predictable methodologies for tying its findings on comparative clinical benefits to its price determinations. A clear framework with a path toward greater clarity will lead to a smoother implementation of the Negotiation Program by reducing stakeholder misperceptions, increasing program stability from administration to administration, and encouraging better evidence development while preventing avoidable impacts on innovation and access.

The implementation burden for CMS in the coming months and years is substantial, and the agency has sought to quickly build its internal capabilities to carry out the Negotiation Program. Alongside CMS's internal implementation capabilities that it has been recently ramping up, CMS could contract the comparative effectiveness assessment process out to an independent organization or entity that would specialize in such activities, with the development of transparent methodologies and technical expertise, as needed. CMS could also support or encourage evaluations from multiple organizations with the goal of more robust assessment.

As part of this framework, describe how real-world evidence development, including evidence related to additional indications, will impact CMS's MFP determinations

Until now, formal health technology assessments (HTAs) of drugs have focused on new products, to help guide initial payer and manufacturer negotiations about coverage and payment. These assessments must rely mostly on premarket evidence, particularly from randomized controlled trials (RCTs). They often include only limited evidence on comparative effectiveness and impacts in real-world populations and conditions of use, and in particular, on diverse subgroups of patients and "off-label" uses, as such questions are not well suited to be answered through traditional RCTs in academic settings. Evidence from well-controlled studies is essential for FDA approval. But such premarket studies generally leave the important real-world questions for Medicare and other beneficiaries unresolved. Consequently, drugs are usually approved with quite limited evidence on comparative effectiveness, with limited evidence on potential impacts in different types of patients, and naturally, with limited prescriber experience. Drugs may be marketed in narrower indications that expand over time, with peak revenues coming some years after the drug's initial adoption. Many drugs have had important indications added long enough after initial marketing, typically five to six years after approval, but sometimes later.² Many drugs are also used "off-label," without such regulatory-grade evidence.

Because the CMS price negotiations will apply to drugs and biologics that have been on the market for at least 7 and 11 years, respectively, CMS has a critically important opportunity to encourage and support the development of much better RWE, both well-designed observational studies and real-world randomized trials (such as clinical trials embedded in routine practice with simpler data collection). To do so, CMS will need to provide more clarity that these types of evidence will have a significant impact on decisions, and provide some illustrative examples of the kinds of studies that would be impactful, just as we have described for the overall CMS comparative effectiveness framework.

More specifically, CMS should provide illustrations of the kinds of RWE that will impact comparative effectiveness and how it will weigh the quality and methods of RWE. There are extensive experiences and frameworks to draw on for this work, both in terms of how RWE can impact key dimensions of comparative effectiveness and how to consider data quality, as well as confounding variables and resulting biases. For example, several international HTA bodies have developed recommendations concerning the use of RWE in comparative effectiveness assessments that may be useful for CMS to

² Sahragardjoonegani B, Beall RF, Kesselheim AS, Hollis A. Repurposing existing drugs for new uses: a cohort study of the frequency of FDA-granted new indication exclusivities since 1997. *J Pharm Policy Pract.* 2021 Jan 4;14(1):3. doi: 10.1186/s40545-020-00282-8. PMID: 33397471; PMCID: PMC7780607.

consider. The United Kingdom’s National Institute for Health and Care Excellence (NICE) published a study design and analysis framework³ for using various types of non-randomized real-world studies in comparative effectiveness evaluations. This framework includes study eligibility criteria that mimic a hypothetical pragmatic trial, comparator requirements, defined follow-up period guidance, and ways for addressing bias and confounding with a detailed analysis plan to describe how the causal effect of interest is to be estimated. The FDA has also published a series of guidances on the use of information from routine clinical practice to derive “fit-for-purpose” RWE to inform its evaluations of product effectiveness.^{4,5}

We understand that the development of a detailed framework is a substantial undertaking. However, CMS could support an iterative process to implement and refine its own framework that would detail how RWE should be used by drug manufacturers as a potentially major part of relevant evidence for the key dimensions of outcomes and safety in its overall comparative effectiveness assessment. This would describe the major kinds of RWE that would be considered—for example, providing guidance on observational target trial approaches and practical randomized studies. It should also discuss ways for ensuring data quality and that data is fit-for-purpose, and ways to address confounding and biases in real-world studies (e.g., use of negative controls). CMS should also describe how the initial (relatively broad) guidance could be refined through further comments and experience—including CMS’s transparent summary of the impact of RWE on each comparative effectiveness assessment.

In particular, CMS should also provide additional clarity on how it intends to treat postmarket studies that add value to a drug through, for example, new formulations and delivery systems that increase patients’ ease of use and thus improve outcomes, and whether such product improvements could lead to upward price adjustments. In fact, the Guidance potentially creates a chilling effect on the development of new product modifications through its expansive definition of “Qualifying Single Source Part D Drugs” (QSSDs), which effectively aggregates all drug versions based on the drug’s active ingredient/moiety, including different New Drug Applications (NDAs) and Biologic License Applications (BLAs), for the purpose of price negotiations, based on the date of the introduction of the first-approved product. We understand that the definition of QSSD is not open for public comment. However, to minimize any adverse effects on the development of important RWE that can add significant value to a selected drug, CMS could clarify what types of evidence it will encourage in this context and whether and how such additional evidence related to product improvements could yield a higher MFP for the negotiated product “group.”

By providing a clearer pathway for implementing and completing RWE studies, and relying on their results, CMS could help shift manufacturer investments toward needed RWE and also reduce delays in drug access for patients who might benefit from this additional evidence generation. For example,

³ “NICE Real-World Evidence Framework,” Published June 23, 2022, <https://www.nice.org.uk/corporate/ecd9/chapter/methods-for-real-world-studies-of-comparative-effects>.

⁴ Food and Drug Administration, “Real World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision-Making for Drugs and Biological Products,” September, 2021, <https://www.fda.gov/media/152503/download>

⁵ Food and Drug Administration, “Real World Data: Assessing Registries to Support Regulatory Decision-Making for Drugs and Biological Products,” November, 2021, <https://www.fda.gov/media/154449/download>

collaborations with The National Patient-Centered Clinical Research Network (PCORnet), which can be used for manufacturer-supported studies, can accelerate RWE studies on important safety or comparative effectiveness questions. Specific collaborations are likely to be possible across different therapeutic areas, building on a range of RWE platforms and resources.

Because RWE generation is often a lengthy and challenging process, it would be helpful for CMS to consider ways in which it can help accelerate the completion of these studies that tend to be more reflective of important Medicare subgroups than traditional RCTs. For example, CMS could facilitate the timely use of CMS data. It could also provide payment incentives for certain data reporting or quality improvement payment adjustments for developing evidence on comparative effectiveness and safety for treatments that are potentially important for the well-being of Medicare beneficiaries. This will likely be a “work in progress” in the early years of the Price Negotiation Program, which is all the more reason to provide a more detailed path forward for how it could be developed.

The IRA is being implemented at an important time in terms of closing these evidence gaps through postmarket, “real-world” evidence. The potential to learn more about drugs after they are on the market is growing, with increasing use of richer digitized and interoperable data, and progress in such areas as precision medicine, postmarket trial platforms, and statistical methods using increasingly rich data. Indeed, CMS has emphasized the goal of enhancing such evidence development to support care for Medicare beneficiaries. However, it is possible that the IRA may have a potentially adverse effect on the use of RWE to inform how to use drugs effectively once they are on the market through label expansions because it may reduce the drug’s price for newer indications that have not yet been on the market for 7 or 11 years (the timeframe for selecting drugs for negotiations for small molecule drugs and biologics, respectively).

CMS should therefore clarify whether and (at least qualitatively) how much the MFP could rise, or if it would be possible to implement a differentiated MFP for the additional indication (something which seems unlikely based on the Guidance) in the event of postmarket label expansions or, since label expansions can take some time, completion and publication of meaningful postmarket studies related to additional populations. Further work by the FDA and other health care stakeholders to clarify faster paths and additional opportunities for timely RWE studies—an area of considerable FDA activity and bipartisan Congressional interest—would encourage and enable product developers and other researchers to contemplate and plan for the systematic execution of such studies to obtain results faster and more efficiently. In addition to providing advance clarity on the Negotiation Program’s expected impact on drug indication expansions, we recommend that CMS support these activities, particularly in instances where postmarket surveillance and/or RWE studies (e.g., point-of-care or pragmatic trials) can support the generation of RWE that is highly relevant and valuable to the Medicare and Medicaid programs and their beneficiaries.

Develop mechanisms to facilitate alternative payment arrangements for drugs that accomplish the intended goals of the IRA

Alternative payment arrangements for drugs, such as subscription or outcome-based payment arrangements, have been proposed and implemented as a mechanism for increasing the health impact

and the value of pharmaceutical products. These models shift from a fee-for-service (FFS) payment structure with high unit prices to payments designed for increased uptake and impact on utilization and outcomes. The implementation of VBP arrangements for drugs might be meaningfully viewed on a spectrum, beginning with payments that remain FFS-based but that are adjusted based on expected value, as determined by existing evidence (e.g., indication-based pricing). Payments with larger shifts from FFS include outcome-based contracts that link payments to a product's actual performance or demonstrated value in a patient or a population, and extend to per-member per-month or whole population "subscription" payments that are not related to the volume of sales at all but rather to access and outcomes in a population.

The IRA could impact adoption of such innovative payment models, which in principle are highly aligned with the IRA goal of lower per-unit drug prices, but also with the equally important goal (from a beneficiary perspective) of increased access and uptake by beneficiaries who would be expected to have better outcomes with the use of the drug – including those who face nonfinancial barriers to access. For example, even though we have more low-cost, effective drugs for heart disease, diabetes, and behavioral health conditions than ever before (with more coming), rates of underdiagnosis and undertreatment remain high, particularly for lower-income and minority populations. CMS should take steps as part of the IRA's implementation to avoid barriers to the development of alternative payment models for drugs, and potentially to encourage them, since their intent is fully aligned with CMS's goals for the IRA as well as for payment reform more broadly in Medicare.

For example, Medicaid Best Price has often been cited as one of the key obstacles for manufacturers to enter into VBP arrangements with payers because providing a substantial rebate to a single commercial payer could require them to extend the same rebate to the entire Medicaid program. Recently-implemented CMS policy changes created Medicaid Best Price flexibilities, such as by allowing manufacturers to report "Multiple Best Prices"⁶ to address these concerns and spur more VBP in the commercial market. Similar concerns may be raised in the context of the impact of VBP arrangements on Medicare MFPs. We believe we can expect less disruption for VBP arrangements from the IRA requirements *so long as such arrangements remain a relatively small part of the market*. Unlike Medicaid Best Price, where a bad result for a single patient in a single contract could potentially reset Best Price for the entire Medicaid market, the prices leveraged in the IRA to determine the ceiling price (such as non-Federal average manufacturer price, or non-FAMP, and Average Sales Price, or ASP) are weighted averages that will be less influenced by low payments in alternative payment models. Furthermore, if a negotiated drug's ceiling price is based on its gross price (i.e., the non-FAMP, which does not include payer rebates), manufacturers and payers may have some flexibility to implement alternative payments via adjusting list prices and rebates without disrupting non-FAMP and thus MFP ceiling calculations.

However, in some cases, alternative payment models for drugs may have advantages over "FFS" drug price reductions alone—and thus could become a larger part of the market. For example, "subscription

⁶ Center for Medicare and CHIP Services, CMS, "Medicaid Drug Rebate Program Notice for Participating Drug Manufacturers, Technical Guidance—Value Based Purchasing (VBP) Arrangements for Drug Therapies Using Multiple Best Prices," March 23, 2022, <https://www.medicaid.gov/prescription-drugs/downloads/mfr-rel-116-vbp.pdf>.

models” that pay for drugs on a population and not per-unit basis could be better aligned with CMS-driven shifts in payments to health care organizations on a risk-adjusted, per-person basis. If payments are further linked to population outcomes (e.g., lower disease complication rates and lower total costs of care – including both drug and non-drug costs), these incentives have the potential to encourage manufacturers to collaborate with providers to further expand access to drugs in ways that are beneficial to patients as well as payers. For example, the administration is encouraging such drug payment reforms to increase access and uptake of curative treatments for hepatitis C infection.

CMS should clarify how alternative payment models for drugs that achieve better outcomes and lower total spending compared to FFS drug payments can be encouraged under the IRA. These arrangements, meant to have a substantially lower price per unit and substantially higher use compared to baseline FFS drug pricing models, could involve a low effective unit price linked to certain steps by drug manufacturers in collaboration with providers, such as outreach to patients who could most benefit from screening and drug treatment. Manufacturers could also receive additional “shared savings” payments when costly complications and non-drug spending for these patients are reduced. If widespread enough, these approaches could reduce the ceiling MFP, even though they lower total health care costs and advance Medicare’s strategic goal of providing more coordinated, accountable care for all beneficiaries.

To address these potential challenges, CMS should consider a regulatory safe harbor or other clarifications for well-designed alternative payment models when the combined drug pricing and access reforms would lead to significantly lower unit drug prices coupled with much higher utilization. CMS should only apply this approach when the manufacturer (and any participating Medicare Advantage or Part D plan) provide clear evidence that per-unit drug net price will be significantly lower than under FFS, with the same or a lower expected unit price than would occur through the MFP, and that, in conjunction with manufacturer, provider, and payer steps (e.g., less or no utilization review) to increase uptake and improve patient outcomes, outcomes will be better as a result of higher utilization with lower total costs of care.

There is a strong policy rationale for exploring these arrangements because they provide incentives for drug manufacturers to work with payers and providers to increase drug access in ways that improve patient outcomes. These payment approaches should also become more attractive under the IRA, since, for the reasons described above, it would provide a pathway for the manufacturer to ramp up sales and reach additional populations faster – but with clear accountability that the increased utilization improves beneficiary outcomes and total Medicare spending.

For the reasons described above, we propose that CMS consider a regulatory safe harbor or similar explicit steps to highlight and encourage such alternative payment arrangements for drugs. In the absence of an exemption for such arrangements that lower total spending, manufacturers could be deterred from implementing alternative payment arrangements with payers and providers who are accountable for total costs of care, despite the alignment of these reforms with overall CMS goals.

Clarify how the manufacturer-specific factors will be used to guide the MFP, and collaborate to support accurate and efficient data collection

After considering the selected drug's price of alternative treatment(s) and its clinical benefit compared to the alternatives, CMS will move to consider a range of manufacturer-specific factors listed in the IRA. These factors include the drug's research and development (R&D) costs, production and distribution costs, revenue and sales volume, patent and regulatory exclusivity protections, and prior federal funding of R&D. Unlike CMS's comparative effectiveness determinations, these factors are not reflective of the selected drug's value, but instead consider its revenues versus its associated costs. This approach has been used less widely in drug price negotiations, and so it would be helpful to implement a stepwise approach to help assure the benefits in terms of reasonable and significant adjustments in the MFP outweigh the potentially costly and complex data collection and analysis.

The IRA provides little detail on how these factors would impact CMS's pricing offer to a manufacturer. Consequently, to limit concerns about cost and uncertainty about potentially valuable investments in drugs, CMS appears to have broad discretion in deciding how to weigh these various data elements when making its pricing offer to the manufacturer. In the Guidance, CMS provides some insight into how these factors could directionally impact the price following the conclusion of the comparative effectiveness assessment. To prevent legal and perception risks, CMS should outline a clear, predictable, and transparent process that would describe how all these factors would be integrated to inform the price negotiation offers and counteroffers. This process should prioritize clarifying data provision and incorporation in MFP calculation based on the likely importance of the factor and the ease of obtaining reliable data to determine impact.

For example, a longer period of market exclusivity for a selected costly drug has a major impact on its revenues; as a result, how CMS considers remaining patent life is likely have a significant impact on the MFP determination. Consequently, CMS should consider prioritizing efforts to distinguish "clinically meaningful" secondary patents from those that were awarded for inventions that add little significant benefit to patients. Related, the agency should prioritize clarifying the standards it will be using to determine when a selected drug's remaining patent life is "too long" to warrant a downward price adjustment.

Conversely, R&D costs and public support for R&D are more challenging to consider and factor into decisions, and at least in many cases, may have less impact on the MFP. First, the cost of capital will be difficult to determine (and could be quite high in the early stages of product development). Furthermore, a manufacturer may not even know the level of private investment in the selected drug if it acquired it from another company, which is the case for most drug products. Further, if a product was acquired, the expected value of any previous public investment was presumably incorporated in the acquisition price, meaning that it was the initial developer and not the acquirer who benefitted financially from said government support.

Finally, the agency plans to rely on several proprietary data elements submitted by the manufacturer in making its pricing adjustments, while maintaining transparency at the same time. It would be helpful for the agency to clarify how much of the negotiation process will be subject to public transparency and

how it intends to explain the MFP without sharing any proprietary information in the event that proprietary factors played an important role in its pricing decision. Providing a clear and detailed summary of the reasons for a final MFP determination, while protecting proprietary information, will be critical for the Negotiation Program's predictability and public support over time.

Clarify additional considerations for implementing the Negotiation Program

Especially in the early years of the Negotiation Program, some enforcement discretion from CMS on implementing the MFP may be appropriate to avoid adverse effects from MFP application. Potential examples where CMS may wish to use its enforcement discretion and exempt a selected drug from MFP application may include the following, non-exhaustive list of examples:

1. A selected drug's comparative effectiveness assessment clearly yields a price that is significantly higher than the MFP ceiling. The drug's manufacturer is also planning additional RWE development and product modifications that will lead to greater patient benefit. Applying the MFP in this case would limit incentives for further evidence and product improvements if the selected drug's price cannot exceed the ceiling. Additionally, in this case, the manufacturer-reported factors do not lead to a price decrease (for example, the manufacturer has incurred high R&D costs with no prior government support, the drug has a short remaining patent life and high costs of production and distribution).
2. An orphan drug exempt from price negotiations as per the IRA's requirements seeking to pursue label extension studies for additional indications. Such studies, which could benefit patients, might not occur given that expanding to additional indications would eliminate the drug's exemption from negotiations.
3. Other areas where innovation is needed but is not occurring to a sufficient degree due to already-existing limited incentives. CMS should monitor for evidence on diminished investment in certain critical therapeutic areas that present their own distinct challenges and barriers after the IRA's implementation, potentially through the dashboard described above.

Aside from care in implementing more aggressive negotiations in cases like these, especially in the early years of the Program, clarifying potential problem areas over time could also provide the basis for developing bipartisan support for any needed future revisions in the IRA, which are typically needed for the long-term success and sustainability of major complex legislation. Despite best efforts, any major new policy initiative may have undesirable consequences. The CMS implementation approach should also include a dashboard at the therapeutic class level to monitor for such consequences and have room to develop plans to address them if necessary. For example, some commenters have raised concerns that the relatively limited time that a manufacturer will now have before price reductions take place may have implications on the launch sequence of drugs, particularly small-molecule drugs, with manufacturers shifting marketing plans toward other highly developed countries first. Relevant RWE and clinical experience can be generated there and subsequently used in the U.S. immediately upon launch to gain broader adoption more quickly than would have occurred otherwise if the manufacturer had to generate that evidence *after* FDA approval. Such decisions, delaying access for U.S. patients,

would allow the manufacturer to capture greater financial benefit of the drug during the full 9 or 13 years before the Medicare price cuts take place. (At the same time, the IRA's Part D redesign to provide more generous drug coverage with no beneficiary payments beyond \$2000 may also have a significant impact on drug uptake and innovation by reducing financial barriers for beneficiaries that limit drug use, with no new tools for plans to negotiate lower prices.)

CMS should track metrics like U.S. versus ex-U.S. initial introductions of new drugs, particularly those that add value according to its own comparative assessment framework. Similarly, the CMS dashboard and regulatory process could track markers of potential issues in other areas where concerns about adverse impacts have been raised, such as diminished investment in therapeutic areas focused on Medicare beneficiaries and small-molecule versus biologic drugs, as well as the timing and extent ("effectiveness") of generic and biosimilar competition. CMS could create a mechanism for stakeholder input into this evolving dashboard and the data that it collects on an ongoing basis, focusing on the beneficiary's perspective.

Finally, CMS should use public comments like these and further internal analysis to clarify its general proposed standard for "robust and meaningful" competition from a generic or a biosimilar drug. Whether this standard has been met determines whether a selected drug should cease being a selected drug – a major regulatory decision point. A standard for how much generic or biosimilar entry has occurred does not appear in the IRA. At the very least, it would be helpful for CMS to establish clear guidelines and illustrations of how this standard could be satisfied, while noting that there are also issues that could prevent effective competition from a follow-on entrant in a way that is beyond their control (for example, certain rebates that may limit competitive entry). Setting the bar too high for this standard might deter generic and biosimilar competition, something which appears concerning as it is from the applications of the IRA's negotiation provisions.

Conclusion

The Duke-Margolis Center appreciates this opportunity to provide feedback to CMS on the Guidance and CMS's consideration of our comments. Our recommendations on the use of high-quality evidence and the design of drug payments to improve outcomes in conjunction with the IRA's Negotiation Program can enable CMS to advance its mission of supporting the high-value, evidence-based, and affordable use of pharmaceuticals. Furthermore, we believe that a clear and predictable initial process for conducting the negotiations and mechanisms for public input and transparency in refining it over time will be important for a predictable and sustainable Negotiation Program and outcome. We and our colleagues would be pleased to provide more information on these issues if that would be helpful. If you have any questions, please contact Nitzan Arad (nitzan.arad@duke.edu) for more information. These comments are those of the authors at Duke-Margolis and are not reflective of the view of Duke University leadership, staff, or other affiliated individuals or organizations.

Sincerely,

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Nitzan Arad – Assistant Research Director, Duke-Margolis Center

Rachele Hendricks Sturup – Research Director, Duke-Margolis Center
Marianne Hamilton Lopez – Senior Research Director, Duke-Margolis Center

DISCLOSURE

Mark B. McClellan, MD, PhD, is an independent director on the boards of Johnson & Johnson, Cigna, Alignment Healthcare, and PrognomiQ; co-chairs the Guiding Committee for the Health Care Payment Learning and Action Network; and receives fees for serving as an advisor for Arsenal Capital Partners, Blackstone Life Sciences, and MITRE.



April 14, 2023

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RE: Initial Guidance on Medicare Drug Price Negotiation Program

Dear Deputy Administrator Seshamani:

Eli Lilly and Company (Lilly) appreciates the opportunity to respond to certain sections of the Initial Guidance (Guidance) on the “Medicare Drug Price Negotiation Program” (Program) but is concerned about its inability to comment on other critical issues, such as the definition of a “qualified single source drug” (QSSD).¹ Lilly is one of the country’s leading innovation-driven, research-based pharmaceutical and biotechnology corporations. Our company is devoted to seeking answers for some of the world’s most urgent medical needs through discovery and development of breakthrough medicines and technologies and through the health information we offer. Ultimately, our goal is to develop products that save and improve patients’ lives.

We appreciate the time constraints under which the CMS has been tasked with implementing this new statutory program but have some concerns that CMS is neglecting to address several key issues. As a member of both Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Industry Organization (BIO), Lilly largely joins those groups in their comments on the Guidance and encourages CMS to carefully consider the input of those organizations. Lilly takes this opportunity to offer the following comments to highlight matters of particular concern and Lilly-specific positions.

As a threshold matter, Lilly is deeply troubled by the language of the statute and this Guidance purporting to classify the process by which CMS sets a “maximum fair price” (MFP) as a “negotiation.” It is not. We also object to being forced to agree that the price, to be dictated by the government via this process, constitutes a “maximum fair price.” This characterization of the price as fair, aside from working a reputational harm, poses a non-trivial legal risk that plaintiffs’ attorneys, or others, will seek to use this “admission” to advance legal claims that other prices charged by manufacturers result in an “unfair” price or a deceptive trade practice. Because these terms are legally defined and prescribed by the Inflation Reduction Act of 2022 (IRA), we will occasionally adopt them for purposes of this letter; however, we do not agree that their use is appropriate or compatible with their plain meaning.

¹ Centers for Medicare & Medicaid Services (CMS), “Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments” (Mar. 15, 2023).

Political euphemism is being used here to steer public opinion away from concerns associated with the harmful and confiscatory impact of price controls, such as their chilling effect on innovation and research, limits on patient choice, and threats to the basic liberty of private parties. The use of these terms, however, will contribute to confused discourse and flawed policy outcomes. The use of the term “negotiation” in the context of this statute and this Guidance feels particularly Orwellian because there are so few indicia of an actual negotiation. Examples include, but are not limited to, the following:

- In a true negotiation, if a seller does not agree to the buyer’s offer price, the seller can walk away, losing the potential business opportunities on just those forgone sales; under the MFP regime, if a seller (the manufacturer) does not agree to the buyer’s (CMS’s) offer price, the seller is required to pay a daily tax to the United States Treasury equal to 19 times the total daily U.S. gross sales of the product in question;
- In a true negotiation, parties sign a contract **after** agreeing to a price term; under the MFP regime, manufacturers must sign a contract **before** agreeing to a price term;
- In a true negotiation, the non-price terms and conditions of a contract are proposed early in the negotiation process such that both sides have more or less equal knowledge of what those non-price terms will be; under the MFP regime, CMS alone knows what the non-price terms and conditions (Program requirements) will be, but the manufacturer does not (at least for the initial year);
- In a true negotiation, both parties can offer revision, clarification, amendment, or customization of the non-price terms and conditions of a contract; under the MFP regime, CMS will publish a “one size fits all” contract of adhesion that manufacturers must sign;
- In a true negotiation, either party may seek redress from an Article III court to redress any legal and equitable claims; under the MFP regime, manufacturers are foreclosed from seeking any form of judicial or administrative review of the most fundamental agency actions;
- In a true negotiation, a seller is free to discuss or describe their experiences with a particular buyer so that other sellers – or the public or Congress – can be on notice as to that buyer’s conduct in negotiation; under the MFP regime, manufacturers are subject to a gag order where CMS is not;
- In a true negotiation, buyers may – but certainly are not required to – turn over any manufacturing or distribution costs, sales forecasts, marketing budgets, or other trade secrets or proprietary data demanded by the buyer; under the MFP regime, CMS requires the submission of all manner of data, some impossible to locate or create;
- In a true negotiation, the buyer cannot threaten the seller with civil monetary penalties (CMPs) of up to \$100,000,000 per item if proprietary information is not turned over; under the MFP regime, these fines, and multiple others, can be wielded against manufacturers – and manufacturers alone.

For these reasons, Lilly respectfully rejects the proposition that the MFP regime establishes a “Negotiation Program,” and we will refer to the process by which the government sets the MFP simply as the “Program.”

Our other substantive comments can be summarized as follows:

- I. We urge CMS to engage in notice and comment for all aspects of its implementation of the Program. Specifically, CMS should (1) solicit comments on section 30 of the Guidance; (2) make proposed text of the Program agreement available for public comment at least 60 days in advance of the first selected drug publication date; and (3) meaningfully respond to and publicly post all comments on all provisions of the Guidance.
- II. CMS should revise the National Drug Rebate Agreement (NDRA) and the Coverage Gap Discount Program Agreement (and work with the Health Resources and Services Administration (HRSA) to revise the Pharmaceutical Pricing Agreement (PPA)) to permit immediate termination of such agreements in the event an MFP cannot be agreed upon by the manufacturer and CMS.
- III. We strongly urge CMS to rescind its policy on identifying distinct QSSDs and instead distinguish between different QSSDs by reference to distinct New Drug Applications (NDAs) or Biologics License Applications (BLAs). Accordingly, CMS should aggregate Medicare expenditures and apply the MFP across only those dosage forms and strengths that are marketed under a single distinct NDA or BLA for each QSSD.
- IV. We ask that CMS be especially solicitous of the special considerations that attach to orphan drugs in implementing the Program.
- V. With respect to the biosimilar delay provision, we recommend that CMS (1) set the deadline by which a biosimilar manufacturer must request a delay closer to the applicable selection date and allow broad supplementation of a timely request; (2) notify manufacturers of its determination prior to the applicable selection date and establish a reasonable mechanism to dispute the determination; (3) request and consider all relevant information; and (4) clarify what circumstances constitute incentivizing a biosimilar delay request.
- VI. We strongly urge CMS to rescind its unlawful bona fide marketing standard. CMS should instead use the definition of “marketed” in the NDRA, which manufacturers already report under the Medicaid Drug Rebate Program (MDRP).
- VII. We urge that CMS notify the manufacturer of any drug that it intends to select for the MFP process in advance of the applicable selection date and afford such manufacturer a reasonable opportunity to dispute the propriety of such intended selection. Additionally, we ask that CMS permit biosimilar manufacturers to ascertain from the agency whether CMS intends to select the applicable reference biologic in advance of the deadline for submitting a delay request to enable informed and efficient decision-making.
- VIII. With respect to the MFP process, we recommend the following:
 - A. CMS should enhance the proposed “consistent methodology and process” for “negotiation” and “renegotiation.” Specifically, we ask that this process include fully bespoke negotiations, consideration of all information submitted, a thorough justification of the initial offer and the response to any counteroffer, and full

opportunity to supplement submitted information where there are material changes or otherwise for good cause shown.

- B. CMS should permit manufacturers to rely on reasonable assumptions in connection with data submissions and provide voluntary explanations of data submissions, as appropriate.
 - C. CMS should establish more detailed safeguards to ensure that confidential commercial information is adequately protected from disclosure. Additionally, CMS's proposed policies regarding use and destruction of information by manufacturers are unlawful, and therefore CMS must abandon them.
- IX. In setting the MFP, we urge CMS account for special considerations by adopting the following recommendations:
- A. CMS should allow manufacturers to submit evidence demonstrating that a price will imperil patient access, and CMS should specify that the MFP will not be set below the lower of either that price or the MFP ceiling price.
 - B. CMS should clarify that it will not set the MFP below the MFP ceiling for any initial price applicability year (IPAY) during which the drug is under patent protection.
 - C. For a small molecule drug, CMS should specify that it will not set the MFP below the MFP ceiling until at least 13 years have lapsed since the drug's approval.
 - D. CMS should specify that the MFP will not be set below the MFP ceiling price where a state uses the MFP as a reference point in setting a price or payment limit outside of the Medicare market. And we ask that CMS specify that such use of the MFP will constitute a "material change" triggering selection for "renegotiation."
 - E. CMS should specify that the MFP will not be set below the MFP ceiling if the selected drug is subject to a value-based purchasing arrangement (VBP) and the multiple Best Prices (BPs) reporting option (MBPRO).
- X. We disagree with CMS's proposal to base the calculation of average Non-FAMP on a calendar year (rather than a federal fiscal year), but we agree that a weighted average is the best – and only appropriate – means of calculating the applicable average Non-FAMP.
- XI. We recommend that CMS use the start of the IPAY, not the date of selection, to measure the date period since approval/licensure to identify whether an "extend" or "long" monopoly drug.
- XII. We concur with CMS that manufacturers should be permitted to provide access to the MFP through a rebate model. However, to ensure the functionality of the model, we ask CMS to specify that rebates are not owed until after all necessary data have been submitted to the manufacturer. We also agree that manufacturers should not be required to provide the MFP to Part D beneficiaries at the point-of-sale directly.

- XIII. We recommend that CMS require Medicare Advantage (MA), MA-prescription drug (PD), and PD plans to require the accurate use of either a 340B or a non-340B claims indicator for Part B and D drugs as a condition of payment of a claim for reimbursement in advance of IPAY 2026.
- XIV. We urge CMS to clarify that selected drugs are not subject to an inflation rebate.
- XV. With respect to CMPs, we urge CMS to finalize its pre-sanction procedural safeguards and to adopt an additional process whereby manufacturers are given advance notice of an intent to impose a CMP and a reasonable opportunity to cure or dispute the deficiency.
- XVI. Finally, we recommend that CMS exclude MFP units from the definition of “unit” for purposes of the Average Sales Price (ASP) calculation.

I. CMS Should Engage in Notice and Comment for All Aspects of Its Implementation of the Program

A. CMS Should Solicit Comments on Section 30 of the Guidance

Although Lilly appreciates that CMS has provided opportunity to comment on many aspects of the Guidance, we are gravely concerned that CMS has not extended such opportunity across **all** components of the Guidance. In particular, Lilly is deeply concerned that CMS has finalized section 30 of the Guidance without opportunity for comment.² It is difficult to envision a more important section of the Guidance on which CMS should solicit comments. Section 30 sets forth foundational policies related to the identification of drugs eligible for an MFP: Among other things, section 30 includes CMS’s approach to distinguishing between different QSSDs. Providing a notice and comment opportunity is a beneficial transparency measure likely to improve implementation of the Program for patients who rely life-saving medicines.

These policies are fundamental to the Program and cut across virtually all aspects of the program’s implementation. CMS’s failure to solicit comment on these critical policies is therefore irreconcilable with the agency’s stated commitment to “prioritiz[ing] transparency and robust engagement” in implementing the program.³

Indeed, because the policies contained in section 30 undergird so many **other** policies described in the Guidance, CMS’s failure to solicit comment on this section casts fundamental doubt as to the meaningfulness of the comment process as a whole. CMS’s solicitation of comment cannot be meaningful if the agency does not seek comments on the foundational components of the Program’s implementation.

Lilly therefore strongly urges CMS to reconsider its decision to deem this section final and open the policies therein to public input. CMS should request stakeholder comments on **all** provisions of the Guidance – including section 30.

² Lilly acknowledges that the policies contained in section 30 of the guidance are final and that CMS is not soliciting comment even after the fact. Nonetheless, Lilly sets forth some of the comments it would have made on section 30 had CMS solicited comment.

³ CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026 at 1 (Jan. 11, 2023).

B. CMS Should Make the Proposed Text of the Program Agreement Available for Public Comment at Least 60 Days in Advance of the First Selected Drug Publication Date

In the Guidance, CMS commits only to making “**reasonable efforts** to make the **final** text of the agreement available to the public before the first selected drug list . . . is published.”⁴ This is facially inadequate. The agency should not merely make such “reasonable efforts.” Rather, CMS should affirmatively commit to making the proposed text of the agreement available for public comment at least 60 days in advance of the first selection date and provide manufacturers the opportunity to offer feedback on the agreement that they may be expected to enter into shortly thereafter.

An opportunity for advance review and comment on the terms of the Program agreement is critical for myriad reasons. Manufacturers are subject to CMPs of \$1 million dollars per day for a violation of a term of the agreement;⁵ they are also subject to a punitive excise tax for failing to enter into the agreement by a specified date.⁶ Under these circumstances, manufacturers are effectively compelled to enter into and abide by the agreement. To give meaning to the agency’s stated intention that “entering into an Agreement is voluntary,”⁷ manufacturers should be given a reasonable opportunity to review in advance and provide comment on the precise terms of the agreement and potentially, in certain cases, negotiate customized terms and conditions that address potential manufacturing, distribution, or other product-specific attributes.

Advance notice will help to ensure that manufacturers are aware of any compliance responsibilities and give them greater time to prepare accordingly. Without advance notice, CMS could put manufacturers in the untenable position of being subject to requirements that are impossible to fulfill due to the agency’s own failure to provide adequate time for manufacturers to establish new processes needed to ensure compliance. Courts have long recognized that “[i]mpossible requirements imposed by an agency are perforce unreasonable” and therefore arbitrary and capricious.⁸ And this risk is especially acute if the agreement imposes requirements that necessitate the development of new or modified systems, require hiring of new staff, or entail entering into new or modified contracts with third parties.

A comment process on the specific terms of the agreement will also serve an equally critical role. It will help to ensure that “interested members of the public [can] communicate information, concerns, and criticisms to the agency”⁹ about an agreement with vast downstream consequences for manufacturers and access to medicines. The need for a comment process is particularly acute because it is vital that the agreement account for market realities. CMS may fail to consider these factors if the agency does not provide opportunity for meaningful engagement by stakeholders.

C. CMS Should Meaningfully Respond to and Publicly Post All Comments on All Provisions of the Guidance

Lilly also strongly urges CMS to respond meaningfully to stakeholder comments on **all** provisions of the Guidance – including section 30 – and thus fully follow through on the agency’s stated

⁴ Initial Guidance at 27.

⁵ SSA § 1197(c).

⁶ Internal Revenue Code (IRC) § 5000D(b)(1)(A).

⁷ Guidance at 27.

⁸ *All. for Cannabis Therapeutics v. DEA*, 930 F.2d 936, 940 (D.C. Cir. 1991).

⁹ *Conn. Light & Power Co. v. NRC*, 673 F.2d 525, 530 (D.C. Cir. 1982).

commitment to transparency and robust engagement. Given the statutory directive to implement the Program in its early years via guidance, as opposed to rulemaking,¹⁰ it is imperative that CMS adopt procedural safeguards that ensure its policymaking is transparent and fair. Inherent in such procedural safeguards is that the agency not only adopt a fulsome comment process, but also respond to comments in a meaningful fashion.

As the D.C. Circuit has observed, “the opportunity to comment is meaningless unless the agency responds to significant points raised by the public.”¹¹ The agency’s timely explanation of how commenters’ information, concerns, and criticisms factored into its final decision-making is what allows the comment process to serve its intended role of facilitating a “genuine interchange” of ideas.¹² The process of responding to discrete points raised by commenters helps to ensure that the agency is carefully considering the feedback it received from the public.

The need for a fulsome and two-sided dialogue is especially compelling here, given the newness and complexity of the issues at hand and the fact that the Program is supposed to reflect a form of negotiation. The Program will have vast ramifications for patients, providers, manufacturers, and other stakeholders across the United States, and the proposals herein represent the agency’s first significant endeavor to fill a largely blank slate. “The interchange of ideas between the government and its citizenry” is what “provides a broader base [to the government] for intelligent decision-making and promotes greater responsiveness to the needs of the people.”¹³ Misinformed implementation here could have especially sweeping negative repercussions with respect to Medicare beneficiary access to needed medicines. Under these circumstances, it is vital that CMS make every effort to maximize transparency and fairness by not merely affording a **full** opportunity for comment on **all** provisions of the Guidance but also **meaningfully responding** to stakeholder feedback, including on section 30 of the Guidance. Further, in furtherance of open government, CMS should publicly post all comments received on this Guidance, as well as others, so that all stakeholders can benefit from the varied perspectives and positions and understand which public policy and practical implementation points CMS finds persuasive.

II. Voluntariness

In Section 40.1, CMS reminds manufacturers of the potentially ruinous excise taxes that may be levied if manufacturers participating in federal healthcare programs do not sign the Program agreement by October 1, 2023 (before any MFP is set). In the next breath, CMS states that participation in the Program is “voluntary” for manufacturer.

At a minimum, we urge CMS to address certain legal and operational issues for manufacturers whose product is selected for the MFP process for IPAY 2026 but that may wish to withdraw from participation in federal healthcare programs. Specifically, CMS should revise the NDRA and the Coverage Gap Discount Program Agreement, and work with HRSA to revise the PPA, to permit immediate termination in the event agreement on an MFP cannot be reached or a manufacturer is dissatisfied with the MFP or the MFP setting process.

¹⁰ SSA § 1198(c).

¹¹ *Ala. Power Co. v. Costle*, 636 F.2d 323, 384 (D.C. Cir. 1979).

¹² *Conn. Light & Power Co. v. NRC*, 673 F.2d 525, 530 (D.C. Cir. 1982) (describing the purpose of notice-and-comment rulemaking).

¹³ *Buschmann v. Schweiker*, 676 F.2d 352, 357 (9th Cir. 1982) (internal quotation marks and citations omitted).

Under the statute, manufacturers that fail to agree to an MFP are deemed non-compliant with program requirements and subject to a punitive excise tax on the first day after the applicable statutory deadline (i.e., August 2, 2024, for IPAY 2026, and November 2 for each IPAY thereafter). The excise tax starts at approximately 200% of a product's daily gross sales in the United States during the first quarter of non-compliance and increases until it reaches 1900%. The excise tax ceases to apply "on the first date on which[:]

- (i) the notice of terminations of all applicable agreements of the manufacturers has been received by [CMS], and
- (ii) none of the drugs of the manufacturer of the designated drug are covered by an agreement under section 1860D-14A [Coverage Gap Discount Program] or 1860D-14C [Manufacturer Discount Program, which will replace the Coverage Gap Discount Program starting in 2025] of the [SSA] [collectively, the Discount Program]."¹⁴

The applicable agreements referenced include agreements under the Discount Program and under the MDRP. Therefore, an alternate to paying the tax is to withdraw all drugs from coverage under Medicare and Medicaid. Thus, as CMS correctly acknowledges in the Guidance, a manufacturer's decision to "enter[] into [a Program agreement] is [intended to be] voluntary." And the Program agreement may be "terminated by either party," at which time the selected drug will no longer be considered a selected drug.

To provide for a modicum of basic fairness and procedural due process, Lilly urges CMS:

- To clarify that it understands "notice of terminations" to refer to the notice required under the termination clause of each applicable agreement; and
- To revise its agreements under the Discount Program and the MDRP, and work with HRSA to revise the PPA, to allow for immediate termination of such agreements in the event that CMS and the manufacturer cannot agree to an MFP for a selected drug under the Program.

CMS should also establish an electronic process by which manufacturers can furnish the agency (and the Internal Revenue Service) with their notice of terminations of the applicable agreements in the event the parties cannot agree to an MFP, and specify that, under such process, the date received for purposes of the suspension of the excise tax is the date the notice is transmitted to the agency.

CMS also states that, "if the Primary Manufacturer of a selected drug elects to enter into an Agreement with CMS . . . , the Primary Manufacturer must submit to CMS [via the Health Plan Management System] all names, titles, and contact information for representatives authorized to execute the Agreement and conduct the negotiation" within "5 days following publication by CMS of the list of selected drugs for an initial price applicability year [September 1, 2023, for the first year of the Program]."¹⁵ We recommend that CMS recast the significance of entering contact information into HPMS. Specifically, a manufacturer's willingness to provide updated names, titles, etc. should not be construed to imply that the manufacturer has "elect[ed] to enter into an Agreement with CMS" but rather should be understood to mean that the manufacturer is "considering whether to enter into an Agreement with CMS." Otherwise, it could be suggested that, for IPAY 2026, a manufacturer would

¹⁴ IRC § 5000D(c)(1)(A).

¹⁵ Guidance at 27.

only have 5 days to “decide” whether to “agree” to a number of new terms and conditions it may have never seen before. That is a wholly unrealistic amount of time to make a decision of the magnitude occasioned by the MFP regime.

Failure to adopt these recommendations renders the Program agreement involuntary. This is because, as noted above, manufacturers that decline to agree to an MFP are subject to a substantial excise tax so punitive it could bankrupt them, the suspension of which occurs only after CMS receives notice of termination of applicable agreements such that the selected drug is no longer subject to such agreements. Under the current applicable agreements, termination does not become effective until a specified period after notice is given. Given the magnitude of the penalties involved, it would be fundamentally unfair to subject a manufacturer to such penalties in the interim. As such, CMS must amend the termination clauses of the applicable agreement to provide for immediate termination in the contemplated circumstance, and it must do so well in advance of August 2, 2024 – i.e., the date on which the excise tax can first begin to accrue for failure to agree an MFP. Notably, under the terms of the Discount Program agreement, termination is effective as of the day after the end of the calendar year if termination occurs before January 30 or the day after the end of the succeeding calendar year if termination occurs on or after January 30.¹⁶ A year-long delay in termination would result in hundreds of millions, if not billions, of dollars in liability. Given the magnitude of the penalties involved, it cannot be said that a manufacturer voluntarily entered into a Program agreement absent a meaningful opportunity to withdraw from the applicable agreements before sanctions are imposed.

III. Identifying QSSDs

A. *CMS Must Rescind Its Policy on Identifying Distinct QSSDs and Instead Distinguish Between Different QSSDs by Reference to Distinct NDAs or BLAs*

Under the Program, CMS selects a QSSD for the MFP process based on the agency’s calculation of “total expenditures” under Part B or Part D for dosage forms and strengths of the drug, and then applies the drug’s MFP to all such dosage forms and strengths.¹⁷ Importantly, the statute does not specify how to make a number of threshold determinations necessary for the fulfillment of these directives, namely:

¹⁶ Coverage Gap Discount Program Agreement, § VIII(d). Similarly, under the terms of the NDRA, termination is not immediately effective. Termination becomes effective on the first day of the first rebate period beginning 60 days after the manufacturer gives written notice. NDRA § VII(a); 83 Fed. Reg. 12,770 (Mar. 23, 2018).

¹⁷ SSA §§ 1192(e)(1), (d)(3)(B), 1196(a)(2). The statute employs different articulations when referring to the versions of the drug that must be taken into account in aggregating Medicare expenditures and applying the MFP. Specifically, section 1192(d)(3)(B) of the SSA refers to aggregation of Medicare expenditures “across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended release formulation, and not based on the specific formulation or package size or package type of the drug.” And section 1196(a)(2) refers to application of the MFP to “different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug.” Regardless, the statutory text makes clear that, whether aggregating Medicare expenditures or applying the MFP, CMS may consider only formulations within dosage forms and strengths of the drug, and not any other formulations. This is so because the statute directs such aggregation and application at dosage forms and strengths of the drug, with all references to formulations appearing only in language qualifying such directives. *See BST Holdings, LLC v. OSHA*, 17 F.4th 604, 613 (5th Cir. 2021) (“To avoid ‘giving unintended breadth to the Acts of Congress,’ [a basic rule of interpretation is to] ‘rely on the principle of noscitur a sociis—a word is known by the company it keeps.’”); *see also FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000) (“It is a ‘fundamental canon of statutory construction that the words of a statute must be read in their context and with a view to their place in the overall statutory scheme.’”).

- How to identify a QSSD and distinguish it from another when selecting a QSSD for the MFP process;
- How to identify “the drug” when aggregating Part B or Part D expenditures across dosage forms and strengths of “the drug;” and
- How to identify “[the] drug” when applying the MFP across dosage forms and strengths of “[the] drug.”

In the Guidance, CMS sets forth an approach to identifying a distinct QSSD by reference to active moiety (drugs) or active ingredient (biologics). Specifically, CMS defines QSSD to include all dosage forms and strengths of drugs or biologics that share the same active moiety or ingredient of the same NDA or BLA holder, respectively, regardless of whether the drugs or biologics are marketed pursuant to distinct NDAs or BLAs. As such, for the first IPAY, CMS will aggregate Part D expenditures across all dosage forms and strengths of drugs or biologics sharing an active moiety or an active ingredient of the same NDA or BLA holder and will apply the MFP across all such dosage forms and strengths.

As explained below, CMS’s approach contradicts the plain language of the statute. By law, CMS is required to identify each QSSD by reference to its NDA or BLA, such that:

- A QSSD is defined by reference to whether the product has a distinct NDA or BLA;
- Expenditures are aggregated across dosage forms and strengths marketed pursuant to a common NDA or BLA; and
- The MFP is applied across the dosage forms and strengths specific to each such NDA or BLA.

CMS’s contrary approach is not merely inconsistent with the statute, but it is also fundamentally unsound as a matter of policy, and risks constraining pharmaceutical and biotechnology innovation through a sweepingly overinclusive interpretation of what constitutes a distinct QSSD. Under the QSSD definition as interpreted by CMS, any innovation related to formulation made post the initial NDA/BLA, which could be meaningfully beneficial to patients, has no significance.

1. Distinct QSSDs Must Be Defined by Reference to Distinct NDAs or BLAs

Under section 1192 of the SSA, only “qualifying single source drugs” are subject to the MFP process. Subject to certain exclusions, “qualifying single source drugs” are defined as:

- Drugs approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act (FDCA), “for which, as of the selected drug publication date with respect to such initial price applicability year, at least 7 years will have elapsed since the date of such approval,” and that are not a listed drug for a drug approved and marketed under an abbreviated new drug application (ANDA) pursuant to section 505(j) of the FDCA (i.e., for a generic); and
- Biologics licensed under section 351(a) of the Public Health Service Act (PHSA), “for which, as of the selected drug publication date with respect to such initial price applicability year, at least 11 years will have elapsed since the date of such licensure,” and that are not the reference product for any biological product licensed and marketed under 351(k) of the PHSA

(i.e., for a biosimilar).¹⁸

The statutory text plainly specifies that a “qualifying single source drug” is defined by reference to each “such approval” or “such licensure,” which starts each seven- or eleven-year clock. As such, the statute requires that a distinct QSSD be defined by reference to a *distinct approval or licensure*, i.e., a distinct NDA or BLA.

CMS’s Guidance takes a contrary approach. The agency says that it intends to treat all dosage forms and strengths of products **with the same active moiety (drug) or active ingredient (biologic)** under applications held by the same primary manufacturer as the same QSSD, **regardless of whether such products are approved or licensed under distinct applications.**¹⁹

CMS’s approach cannot be reconciled with the statutory definition of QSSD.²⁰ Congress **explicitly** defined a QSSD by reference to “such approval” and “such license” to denote that QSSDs **must** be distinguished by their distinct approvals or licensures. As such, CMS’s policy is fundamentally at odds with the language of the statute, which evidences Congress’s clear intent to distinguish QSSDs by reference to distinct “approvals” or “licensures” – that is, whether they have a distinct NDA/BLA.

The statute reinforces Congressional intent to distinguish QSSDs based on their NDAs or BLAs by specifying in the QSSD definition that a QSSD that is a Part D drug must meet the “covered Part D drug” definition in the Medicare statute.²¹ The Medicare statute, in turn, defines a “covered Part D drug” by reference to the “covered outpatient drug” definition in the MDRP statute.²² And, under the MDRP statute, a “covered outpatient drug” is defined by reference to a Food and Drug Administration (FDA) approval or licensure under an NDA or BLA.²³ Indeed, the government itself recognizes as much.²⁴

The MDRP statute provides for only one exception to the rule that a drug or biologic is defined by reference to its NDA or BLA, and Congress specifically amended the statute to provide for such exception. Congress affirmatively amended the MDRP statute to treat a line extension as the same drug as its predecessor version(s), even when approved under a distinct NDA or BLA, when calculating the line extension’s Medicaid rebate amount.²⁵ Under the Program, no similar statutory exception exists, reinforcing the conclusion that Congress intended that a QSSD be identified by its NDA or BLA.²⁶ Congress clearly would have said otherwise had it intended any other result. Indeed, elsewhere in the IRA, Congress did do so. In the provisions governing the IRA’s Part D inflation rebate

¹⁸ *Id.* § 1192(e)(1). Selected drug publication date is a term of art meaning that, with respect to each IPAY, February 1 of the year that begins 2 years prior to such year. *Id.* § 1191(b)(3).

¹⁹ Guidance at 8.

²⁰ *Love v. Tippy*, 133 F.3d 1066, 1069 (8th Cir. 1998) (it is well-settled that “if a statute is unambiguous the statute governs”).

²¹ SSA § 1192(e).

²² *Id.* § 1860D-2(e)(1).

²³ *Id.* § 1127(k)(2).

²⁴ *See, e.g.*, Reply Brief in Support of Def.’s Cross-Mot. for Summ. J., *Ipsen Biopharms., Inc. v. Price*, at 19 (D.D.C. Oct. 30, 2017) (“CMS has long interpreted the Medicaid Drug Rebate provisions of the [SSA] such that each covered outpatient drug is identified by its [NDA] number”).

²⁵ *See* Patient Protection and Affordable Care Act of 2010, Pub. L. No. 111-148, § 1206 (Mar. 23, 2010) (codified at SSA § 1927(c)(2)(C)).

²⁶ *See Franklin Nat’l Bank v. New York*, 347 U.S. 373, 378 (1954) (there is “no indication that Congress intended” a particular interpretation where it has previously authorized such interpretation “by express language” but has not done so in the instant case).

program, Congress expressly referenced the MDRP statute's line extension provision to enable the grouping of products across NDAs or BLAs.²⁷ By contrast, Congress pointedly declined to do likewise in defining a QSSD.

Although the interpretive "inquiry begins with the statutory text, and ends there as [well because] the text is unambiguous,"²⁸ Lilly notes that there are a host of additional factors that lend further support for the conclusion that Congress intended QSSDs to be distinguished on the basis of distinct NDAs/BLAs.

First, FDA's framework for approving products via distinct applications strongly supports the use of distinct NDAs/BLAs as the standard for distinguishing between QSSDs. As a general matter, prescription drugs and biologics may be marketed only if approved or licensed by FDA.²⁹ Manufacturers seeking approval of a new drug must submit data to FDA sufficient to satisfy the safety and effectiveness standard for approval of an NDA³⁰ And manufacturers of a new biologic likewise must demonstrate to FDA the safety, purity, and potency of the product in order to be licensed under a BLA.³¹

FDA has spoken directly to the circumstances under which a change to an approved product can be approved by submitting a supplement to an already-approved NDA/BLA, and that for which a separate NDA/BLA should be submitted instead.³² It is reasonable and appropriate to rely on these FDA standards, such that a product approved/licensed via a separate NDA/BLA (as opposed to by a supplement to an already-approved NDA/BLA) is considered a distinct QSSD. For example, FDA directs manufacturers of a new active ingredient, e.g., a different salt, ester, or complex of an approved moiety, to submit a separate application.³³ On the other hand, a proposed different strength should be approved via a supplement.³⁴ And different container sizes and package types of a drug with the same indication and route of administration are all approved under a common application.³⁵ Certain changes in dosage form or route of administration may be approved via a supplement, but others should be approved via a separate application.³⁶

Second, a distinct NDA/BLA standard is consistent with the balance the statute strikes between the often-competing interests in encouraging pharmaceutical and biotechnology innovation and reducing prescription drug costs. The statute seeks to address this tension by, among other things, establishing a period of time after approval or licensure during which a product is not eligible for selection for the MFP process, thus preserving an incentive for the manufacturer to research and develop next-generation products. Similarly, distinguishing between products by the NDA/BLA under which they are approved reflects a balance between more significant changes (i.e., those requiring a new NDA/BLA), yielding distinct products for MFP setting purposes, and less significant

²⁷ SSA § 1860D-14B(b)(5)(B).

²⁸ *BedRoc Ltd., LLC v. United States*, 541 U.S. 176, 177 (2004).

²⁹ 21 U.S.C. § 355(a); 42 U.S.C. § 262(a)(1)(A).

³⁰ 21 U.S.C. § 355(c),(d); 21 C.F.R. §§ 314.105, 314.125.

³¹ 42 U.S.C. § 262(a)(2)(C); 21 C.F.R. §§ 601.2(a), 601.4(a).

³² FDA, Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees (Dec. 2004), available at <https://www.fda.gov/media/72397/download> (Submitting Separate Marketing Applications Guidance).

³³ *Id.* at 3.

³⁴ *Id.* at 4.

³⁵ *Id.*

³⁶ *Id.* at 3.

ones (i.e., those approved under a supplement to an already-approved application), which are appropriately considered modifications of the same product. Any standard that does not reflect this distinction contravenes the balance Congress crafted by putting next-generation products at risk of being subject to MFP setting on an unduly short (and potentially immediate) time frame³⁷ Accordingly, the sweeping, extra-statutory approach set forth in the Guidance risks dramatically discouraging development of next-generation products.

Lastly, CMS's approach is also unnecessarily complicated. Defining each QSSD by reference to its NDA or BLA makes practical sense. It establishes a readily administrable bright line test for all parties under the Program. CMS will be able to easily identify the relevant dosage forms and strengths of a selected drug for purposes of aggregating Medicare expenditures and applying the MFP, and manufacturers will be able to confidently track the 7- or 11-year timeline from the NDA/BLA approval/licensure date for selection eligibility and make research and development decisions accordingly. By contrast, the approach in the Guidance adds unnecessary complexity to what Congress intended to be an easily administrable statutory standard.

For the foregoing reasons, Lilly vigorously disagrees with CMS's stated approach to identifying a QSSD for legal and policy reasons. We urge CMS instead to define each "qualifying single source drug" by reference to its NDA or BLA, as required by the statute and the dictates of sound public policy.³⁸

2. CMS Must Aggregate Part B or Part D Expenditures on a QSSD Across Only Those Dosage Forms and Strengths That Are Marketed Under the Distinct NDA or BLA of Such Drug

A necessary corollary to the requirement that each QSSD be defined by reference to its distinct NDA or BLA is that CMS must aggregate Medicare expenditures across only those dosage forms and strengths of the QSSD that are marketed under the applicable NDA or BLA. This follows from the statutory definition of "negotiation-eligible drug," which is defined as a QSSD that is among the 50

³⁷ This is the same balance between encouraging innovation and reducing drug costs that the Hatch-Waxman Amendments to the FDCA reflect by granting 5-year and 3-year exclusivity to innovative products, but then allowing easy market entry for generics after exclusivity expires. *See Amarin Pharm. Ir. Ltd. v. FDA*, 106 F. Supp. 3d 196, 198 (D.D.C. 2015) ("[T]he [Hatch-Waxman] Act sought to balance two competing policy goals: (1) encouraging the development of generic drugs to increase competition and lower prices in the pharmaceutical industry, while (2) maintaining incentives for pharmaceutical companies to invest in innovation and the creation of new drugs."); *Abbott Labs. v. Young*, 920 F.2d 984, 985 (D.C. Cir. 1990) ("Congress struck a balance between expediting generic drug applications and protecting the interests of the original drug manufacturers.").

³⁸ As CMS itself acknowledges, the agency must apply its definition of "qualifying single source drug" across all uses of such term in the statute. *See* Guidance at 10. Accordingly, if (contrary to the plain language of the statute) CMS maintains that products that share the same active moiety (drugs) or the same active ingredient (biologics) are the same QSSD, Lilly agrees with CMS that the market entry of a generic or biosimilar for any of such product must necessarily disqualify *all* such products from treatment as a QSSD. *See id.* Any other approach would be irreconcilable with CMS's stated approach to identifying a "qualifying single source drug." *See, e.g., Nat'l Credit Union Admin. v. First Nat. Bank & Tr. Co.*, 522 U.S. 479, 501–02 (1998) (a basic canon of interpretation is that similar or identical language must "be accorded a consistent meaning"). Importantly, CMS cannot bootstrap itself out of this outcome through its unlawful bona fide marketing standard for determining when a generic or biosimilar is marketed. *See* Section IV.

QSSDs with the highest total expenditures under Part B or Part D during a specified period.³⁹ To calculate total expenditures on a QSSD, the statute instructs that CMS must “use all data that is aggregated across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended release formulation, and not based on the specific formulation or package size or package type of the drug.”⁴⁰

Because the statute requires QSSDs to be distinguished by reference to their distinct NDAs/BLAs, it necessarily follows that total Part B or Part D expenditures must similarly be aggregated by distinct NDA/BLA. The statute could not be clearer on this point. It requires expenditure data to be “aggregated across dosage forms and strengths of **the drug**, including new formulations of **the drug**, such as an extended release formulation, and not based on the specific formulation or pack size or package type of **the drug**” to determine whether a QSSD is among the highest Medicare expenditure QSSDs during a specified period and thus an MFP-eligible drug.⁴¹ “The drug” can only refer to the QSSD, which, for the reasons stated above, must be defined by its NDA/BLA. It follows, then, that references to the “dosage forms and strengths of the drug” are to the various dosage forms and strengths that are approved under the given NDA or BLA. Further, the succeeding phrase – starting with “including” – necessarily presents “new formulations” as examples of the broader category of products that the phrase qualifies (i.e., “dosage forms and strengths of the drug”). Put differently, the word “including” limits the new formulations of the QSSD (as identified by its NDA or BLA) for which CMS may aggregate Medicare expenditures to a subset of formulations – those related to a change in dosage form or strength. And, as noted above, this interpretation is entirely in keeping with the distinct NDA/BLA standard, as distinct dosage forms and strengths, including new formulations thereof, may indeed be approved under a single application.⁴²

Thus, CMS must aggregate Medicare expenditures across only those dosage forms and strengths (including any new formulations thereof) marketed under the applicable NDA or BLA in determining whether a product is MFP-eligible. This approach is mandated by the language of the statute, reflects a logical and coherent approach to its implementation, and gives effect to the Congressional intent underlying the MFP regime overall.

3. CMS Must Apply the MFP Across Those Dosage Forms and Strengths Approved Under the NDA or BLA of the Selected QSSD

The statute also directs CMS to adopt “procedures to compute and apply the maximum fair prices across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug.”⁴³ In the Guidance, CMS says that it will apply the MFP across all dosage forms and strengths of a given active moiety or active ingredient whose approvals or licensures, respectively, are held by the same primary manufacturer.⁴⁴ However,

³⁹ SSA § 1192(d). In some cases, a drug may be reimbursed under both Part B and Part D depending on where it is administered or dispensed. Because the statute distinguishes between drugs reimbursed under Part D and those reimbursed under Part B, expenditures under each part are aggregated separately for purposes of determining MFP eligibility.

⁴⁰ *Id.* § 1192(d)(3)(B).

⁴¹ *Id.* § 1192(d) (emphasis added).

⁴² We note that some changes in dosage form may be approved via a supplement to an already-approved NDA or BLA, while others require submission of a new application. Submitting Separate Marketing Applications Guidance at 3.

⁴³ SSA § 1196(a)(2).

⁴⁴ Guidance at 8.

just as CMS musts define distinct QSSDs by distinct NDAs or BLAs, and must aggregate Medicare expenditures for purposes of identifying MFP-eligible drugs across dosage forms and strengths within a given NDA or BLA, so, too, must CMS compute and apply the MFP across the dosage forms and strengths within the NDA or BLA of the selected QSSD. This necessarily follows from the statutory text, which plainly directs that the MFP be applied across dosage forms and strengths of such drug. The admonition that follows – to ignore specific formulations in doing so – can be logically understood to mean only that, in applying the MFP across dosage forms and strengths, the fact that there may be multiple specific formulations of those dosage forms and strengths does not alter such directive.

CMS should also recognize that manufacturers might be forced discontinue to making certain product presentations if the MFP, which is set for a molecule regardless of product presentation, renders specific product presentations no longer economically viable. This is most likely to undermine patient convenience and potentially patient adherence, further arguing for CMS to take a more granular approach to its definition of QSSD.

B. The Orphan Drug Exclusion from the Definition of QSSD

Under section 1192(e)(3)(A) of the SSA, drugs that are “designated as a drug for only one rare disease or condition . . . and for which the only approved indication (or indications) is for such disease or condition” are excluded from the QSSD definition and therefore ineligible for selection for the MFP process.⁴⁵ In the Guidance, CMS says that it will use the Orphan Drug Product designation database and the FDA approvals database (Drugs@FDA) to determine whether a drug meets the requirements of this orphan drug exclusion.⁴⁶

As a threshold matter, we note that, in making a determination based on the above FDA resources, CMS should consider only a drug’s orphan designation(s) **at the time of selection**. FDA regulations allow a manufacturer to voluntarily withdraw a requested or granted orphan designation at any time.⁴⁷ FDA publicizes the withdrawal, and any benefit associated with the designation terminates.⁴⁸ With that in mind, CMS should look **only** at orphan designation(s) at the time of selection, and should not look to any previous designation that has been withdrawn when determining whether a drug qualifies for the orphan drug exclusion.

Lilly is concerned CMS’ interpretation of the orphan drug exemption will discourage drug sponsors from developing their product for additional disease states and undermine the intent of the Orphan Drug Act (ODA). CMS’s interpretation of the IRA makes products eligible for negotiation as soon as they have been designated under section 526 of the FD&C Act for more than one orphan disease – even if the drug is not actually FDA approved (or indicated) to treat more than one of the designated orphan diseases. For example, designating a drug under section 526 of the FD&C Act as a rare disease drug is done very early in the drug development process and a key part in unlocking critical ODA incentives such as research funding for clinical research to help de-risk this phase of drug development. However, an orphan designation does not allow the company to market the drug because it has not yet been shown to be safe and effective to treat that specific condition and therefore has not been approved under section 505(c) of the Food Drug and Cosmetic (FD&C) Act or

⁴⁵ SSA § 1192(e)(3)(A).

⁴⁶ Guidance at 11.

⁴⁷ 21 C.F.R. § 316.24(d).

⁴⁸ *Id.*

licensed under section 351(a) of the Public Health services (PHS) Act for that disease. In fact, FDA's Orphan Drug Designations and Approvals database currently contains 6,445 orphan drug designations (including withdrawn designations) compared to only 1130 approved orphan indications, demonstrating that a large number of orphan drug designations do not result in any FDA-approved indications.

Lilly believes that the language of section 1192(e)(3), due to the manner in which it was drafted, is ambiguous and therefore open to CMS interpretation. CMS states that to qualify for the orphan drug exclusion, "the drug or biological product must (1) be designated as a drug for only one rare disease or condition under section 526 of the FD&C Act and (2) be approved by the FDA for only for one or more indications within such designated rare disease or condition." This two-prong test, embodying two separate and distinct criteria, is a possible interpretation of the statute. But under the canons of legislative drafting, if the congressional authors had intended the two clauses to be read ***independently***, the proper legislative drafting would have structured the two clauses separately and in sequence. Instead, Congress did not separate the clauses, intending them to be read ***together***: that a drug designated for a given "rare disease or condition" has "only [one] approved indication" or multiple "approved... indications" ***within the scope of that designation***. CMS substantiates this plain meaning of the provision in accepting that an orphan drug with ***multiple*** ("one or more") FDA-approved indications qualifies for the exemption provided all such approved indications are within the scope of a ***single*** ("only one") ***designation***.

The cardinal rule of statutory construction is that the whole statute should be drawn upon as necessary, with its various parts being interpreted within their broader statutory context in a manner that furthers statutory purposes. The proper interpretation of the orphan drug exclusion "in a manner consistent with [the] legislative purposes" of the Program preserves an intentionally narrow class of qualifying orphan drugs determined upon the basis of a drug's FDA approval history – not on orphan drug designations which have no bearing on, or applicability to, prescription drug marketing or pricing. We encourage CMS to revise its guidance to reflect a sound statutory interpretation more fully in line with congressional intent.

Lilly is also concerned about the potential chilling effect residual uncertainty about CMS's implementation of the orphan drug exemption will have on rare disease drug development. Due to the complexity and long timeline from initial drug discovery and early research and development to full FDA approval, drug sponsors are making decisions now that will impact their drug development pipeline for decades to come. Remaining uncertainty about if, when, and how drugs will become negotiation eligible creates business risks that work as strong disincentives to develop drugs for the limited populations impacted by orphan diseases. For instance, CMS has remained silent as to when orphan drugs that receive an FDA approval for a second disease and therefore loose eligibility for the orphan drug exemption would become negotiation eligible. Qualifying single-source drugs must have been approved at least 7 years and qualifying single-source biologics must have been licensed at least 11 years to qualify, but CMS has not yet clarified if the 7 or 11 years will be counted beginning on the date of the FDA approval for the second disease that made the product negotiation eligible, or based on the first orphan drug approval. CMS should clarify that obtaining additional designations for a small molecule or biologic will not make a drug negotiation eligible until the drug has been approved by FDA for 7 or 11 years to treat the second disease or condition and in doing so, would provide meaningful incentives for continued orphan drug development.

In addition, Lilly is concerned that there may be circumstances where the FDA resources that CMS will rely upon ***will not be sufficient*** to identify a product as qualifying for the orphan drug exclusion.

In particular, FDA's Orphan Drug Product designation database and the FDA approvals database will not identify a drug that has one orphan drug designation and is approved only for indications under that designation – but that has **not been granted orphan exclusivity**.

In this situation, the above FDA resources will not reflect the fact that an approved indication is within the scope of the orphan drug designation and therefore meets the statutory requirement for exclusion from the MFP process. One example where this can happen is when the designated drug has the same active moiety or active ingredient and is seeking approval for the same indication as an already-approved drug. If the designated drug is not “clinically superior” to the already-approved drug, the drug will not qualify for orphan exclusivity. Still, the approved indication is indisputably within the scope of the orphan drug designation, and the drug therefore unambiguously qualifies for exclusion under the statute; nothing in the statute requires that a drug have (or have had) orphan exclusivity in order to qualify for exclusion from MFP setting.

The Guidance does indicate that the agency will consult with FDA as needed.⁴⁹ However, given that there may be circumstances where CMS cannot determine from FDA's databases whether an indication falls within an orphan designation, CMS also should affirmatively allow manufacturers to provide evidence that an indication is within the scope of their drug's orphan designation. Specifically, we ask CMS to establish a pathway by which manufacturers of orphan drugs approved for qualifying indications that are not identified in the relevant databases can work with FDA and/or CMS to demonstrate that an indication falls within an orphan drug designation. CMS should consider written communications with FDA during the review and approval process or written confirmation from FDA regarding the orphan disease for which the drug is designated and the indication for which the product is approved to be acceptable evidence. Affording manufacturers the opportunity to participate in a process to ensure that eligible orphan drugs are excluded from selection for the MFP process is in keeping with overarching policy goals favoring protection of orphan drugs. It will also be more efficient for CMS, as it provides greater flexibility without the agency needing to expend its own resources consulting with FDA each time FDA's public databases are inadequate to verify a product's eligibility for the orphan drug exclusion.

C. Delayed Selection of Biologics on Account of Anticipated Biosimilar Market Entry

Under Section 1192(f) of the SSA, CMS may delay selection of a reference biologic for the MFP process where, among other things:

- The reference biologic that would have been selected for the MFP process would have been an extended-monopoly drug;⁵⁰
- The delay is requested by the sponsor of a pending or approved BLA for a biosimilar of the reference biologic before the date that would otherwise be the selection date of such reference biologic;⁵¹ and
- There is a high likelihood that the biosimilar will be licensed and marketed within two years of what would otherwise have been the reference biologic's selection date.⁵²

⁴⁹ Guidance at 11.

⁵⁰ SSA § 1192(f)(1)(A). See Section VIII(C) for a discussion of the extended-monopoly drug definition.

⁵¹ *Id.* § 1192(f)(1)(B)(i)(1).

⁵² *Id.* § 1192(f)(1)(A).

If, after a first year of delay, the biosimilar has not launched, the biosimilar manufacturer may request a second year of delay before the selection date that follows what would otherwise have been the reference biologic's selection date.⁵³ If the biosimilar comes to market within two years of what would otherwise have been the reference biologic's selection date, the reference biologic will not be eligible for selection for the MFP process. If a second year of delay is not granted or the biosimilar does not come to market within two years of what would otherwise have been the reference biologic's selection date, the reference biologic manufacturer will be required to pay retrospective rebates to CMS.⁵⁴

CMS's Guidance sets forth the agency's implementation of this delay request process. As detailed below, Lilly urges CMS to make certain modifications or clarifications with respect to the process outlined in the Guidance. Specifically, CMS should:

- Revise the Guidance to afford a biosimilar manufacturer a meaningful opportunity to request a delay, set the deadline by which a biosimilar manufacturer must request a delay as close as reasonably possible to the applicable selection date, and permit the biosimilar manufacturer to broadly supplement a timely request with any late-breaking information or otherwise for good cause;
- Notify biosimilar manufacturers of its determination as to a delay request prior to the selected drug publication date and establish a mechanism by which manufacturers can reasonably dispute the determination;
- Permit the biosimilar manufacturer to submit for CMS's consideration any information relevant to a determination of whether there is a high likelihood that the biosimilar will enter the market within two years of what would otherwise be the reference biologic's selection date; and
- Clarify the circumstances where an agreement will be considered to incentivize a biosimilar manufacturer to request a delay.

1. It Is Critical That CMS Afford a Meaningful Opportunity to Request a Delay, Set the Deadline for a Delay Request Closer to the Applicable Selection Date, and Allow Broad Supplementation of a Timely Request

Lilly believes that CMS should respect the intent of the statute to allow market-based competition to lower drug prices and there we strongly oppose the proposed delay request timelines and procedures outlined in the Guidance. In order to make the delay request process as meaningful and accurate as possible, CMS should set reasonable timelines that afford a biosimilar manufacturer a meaningful opportunity to request a delay. And, to ensure that the agency has the most up-to-date and accurate data as it evaluates delay requests, CMS should designate a delay request submission deadline that is closer to the applicable selection date. For the same reason, CMS should allow biosimilar manufacturers to broadly supplement their timely delay requests with additional information.

The statute requires a biosimilar manufacturer to request a delay "at a time . . . specified by the Secretary" prior to the selected drug publication date."⁵⁵ For IPAY 2026, the Guidance requires a

⁵³ *Id.* § 1192(f)(1)(B)(i)(2).

⁵⁴ *Id.* § 1192(f)(2)(B)(ii), (C).

⁵⁵ *Id.* § 1192(f)(1)(B)(i).

biosimilar manufacturer to notify CMS of its intent to submit a request by May 10, 2023.⁵⁶ Within five business days (i.e., by May 17, 2023), CMS will provide the manufacturer a fillable template and access to a manufacturer-specific Box folder.⁵⁷ The biosimilar manufacturer must then complete and upload the template and furnish all supporting documentation by May 22, 2023, only **three business days** from receipt of the template and access to the agency's Box folder. As such, CMS is requiring manufacturers to rush to prepare and submit delay requests, even though the submission deadline is set **over three months** in advance of the selected drug publication date.

Lilly is concerned that CMS's unreasonably accelerated and truncated timelines will inhibit the meaningfulness of the delay request process and will ultimately imperil the incentives for biosimilar competition that Congress intended to foster by establishing such process. This risk is only exacerbated because CMS says that it will automatically deny delay requests deemed "incomplete." There is no defensible justification for so significantly truncating the window during which manufacturers must prepare and submit delay requests, especially given the complex and multi-factorial information that must be submitted in support of such requests.

Worse still, the delay request timeline and process set forth by CMS risk **undermining the accuracy** of CMS's "high likelihood" determination. An informed determination of whether there is a "high likelihood" of timely biosimilar market launch should be based on the **most current information available**, and, necessarily information will be more mature closer to the selected drug publication date. Yet CMS's policy is to require manufacturers to submit the request **over three months in advance** of the selected drug publication date. And the request **cannot** be supplemented, with only very limited exception for updates as to whether the BLA has been accepted or approved by FDA.⁵⁸

The result is a process that includes no mechanism by which CMS can broadly account for late-breaking material developments that may dramatically impact the likelihood of a timely launch. This is concerning because the information bearing on whether a biosimilar is highly likely to be licensed and marketed within the specified period is subject to rapid and potentially unanticipated changes, and such determination is an amalgamation of numerous considerations, each with the potential to fluctuate, including:

- FDA's views of the data and other information submitted in the BLA to meet the requirements for licensing of a biosimilar;
- Communications from FDA about the status of the BLA, which inform whether and when the biosimilar manufacturer can expect licensure;
- The biosimilar manufacturer's production and distribution arrangements and progress, which inform whether and when the biosimilar manufacturer will be in a position to commercially manufacture and distribute a licensed product.⁵⁹

In order for CMS to maximize the accuracy of its delay request determinations, CMS **must** have (and rely on) the most current information available that bears on whether there is high likelihood that a biosimilar will launch within the specified period. As noted above, CMS should therefore (1) set the delay request deadline as close as administratively feasible to the selected drug publication date and (2) allow manufacturers to broadly supplement a timely request with late-breaking, material

⁵⁶ Guidance at 21.

⁵⁷ *Id.*

⁵⁸ Guidance at 23.

⁵⁹ See Section IV for a discussion of the identification of the appropriate market date.

information or for otherwise for good cause shown. This will allow CMS make more informed biosimilar launch likelihood determinations, while eliminating unnecessary timing barriers that can impede the ability of biosimilar manufacturers to access the delay request process in a meaningful fashion.

Ensuring that the information before the agency is not outdated or incomplete will also create efficiencies for the agency because it will reduce the likelihood that CMS erroneously concludes that there is a high likelihood that a biosimilar will launch within the specified period, such that CMS will be obligated to administer the payment of rebates by the reference biologic manufacturer when the biosimilar does not timely launch. CMS can avoid unnecessarily administering such payments, and the resulting needless inefficiency, by using the most current information available – i.e., by (1) setting the delay request deadline as close as administratively feasible to the selected drug publication date and (2) allowing manufacturers to broadly supplement a timely request with late-breaking, material information or for good cause.

2. CMS Should Notify Biosimilar Manufacturers of Its Determination as to a Delay Request Prior to the Selected Drug Publication Date and Establish a Mechanism by Which Manufacturers Can Reasonably Dispute the Determination

Under the Guidance, CMS will not inform a biosimilar manufacturer that submits a delay request that its request is denied until **after** the selected drug publication date.⁶⁰ This means that biosimilar manufacturers have no means to challenge erroneous “high likelihood” determinations. As noted above, this is particularly problematic given the unreasonably accelerated and truncated timelines for requesting the delay described in the Guidance. Accordingly, Lilly recommends that CMS revise its approach. CMS should notify a biosimilar manufacturer that it intends to deny its request in **advance** of the selected drug publication date and establish a mechanism by which manufacturers can reasonably dispute the agency’s determination before the selection of a reference biologic occurs.

3. CMS Should Request and Consider All Information Relevant to a Timely Biosimilar Launch Likelihood Determination

Section 1192(f) of the SSA specifies that a biosimilar manufacturer must submit certain information to support a request for a delay. Notably, section 1192(f)(1)(B)(ii)(I) provides that such a submission contain the contents described in subclauses (aa) and (bb):

- **Subclause (aa)** provides for the Secretary’s consideration of “information and documents **necessary** for the Secretary to make determinations [whether a delay should be granted], as specified by the Secretary, and **including**, to the extent available” the items described in **subclause (III)** of section 1192(f)(2)(B)(ii),⁶¹, namely:
 - “The manufacturing schedule for such biosimilar biological product submitted to [FDA] during its review of the application” and “[d]isclosures [in Securities and Exchange Commission filings] that pertain to the marketing of such biosimilar biological product, or comparable documentation that is distributed to the

⁶⁰ Guidance at 24.

⁶¹ SSA § 1192(f)(1)(B)(ii)(I)(aa) (emphasis added).

shareholders of privately held companies.”⁶²

- **Subclause (bb)** provides for the Secretary’s consideration of “all agreements related to the biosimilar biological product filed with the Federal Trade Commission or the Assistant Attorney General pursuant to subsections (a) and (c) of section 1112 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003.”⁶³

The structure of section 1192(f) therefore makes clear that Congress intended for CMS to consider the **full range of relevant information** necessary to make a “high likelihood” determination **based on all of the information submitted under subclause (aa), rather than solely the specific subset of information cross-referenced in such subclause**, i.e., the information described in subclause (III). By contrast, CMS’s Guidance improperly limits the universe of evidence that CMS will consider when evaluating whether the “high likelihood” standard is satisfied by providing that such evaluation will be performed only under **section 1192(f)(3)**, which limits the information on which an evaluation is based to the information described in subclause (III) and subclause (bb). **The additional information under subclause (aa) that, by statute, is “necessary” to determinations whether a delay should be granted is unaccounted for.**

The analysis must start with section 1192(f)(3), which specifically references information and documents to be considered in making the “high likelihood” determination: those described in subclause (III) and subclause (bb). The Guidance appears to indicate that section 1192(f)(3) represents the only pathway to a high likelihood determination and therefore that consideration of information is limited to these two categories of information.

This approach is contrary to the text and structure of the statute, which clearly contemplates that the test described in section 1192(f)(3) be **only one, non-exhaustive means** of satisfying the “high likelihood” standard. This follows from the plain language of subclause (aa), which directs manufacturers to submit information and documents that are “**necessary**” to a high likelihood determination “**including**” – but not limited to – those described in subclause (III).

The use of the word “including” is telling. “[T]he verb to include introduces examples, not an exhaustive list.”⁶⁴ As such, subclause (aa) **must** mean that there is a universe of information—beyond that articulated in subclause (III) – that **must** be considered as part of the “high likelihood” determination, especially given that the statute characterizes such information as “necessary” to such determination.

The necessary implication is that the “high likelihood” test articulated in section 1192(f)(3) **cannot** be the only means of demonstrating a high likelihood of timely biosimilar market launch, because, as noted, **that** test is limited to an evaluation of only certain specified categories of information (e.g., that described in subclause (III)). Any other interpretation would render the broad and mandatory information submission language in subclause (aa) completely superfluous: Manufacturers would be required to submit the full universe of information “necessary” to make a “high likelihood” determination, but the agency would arbitrarily disregard a subset of such “necessary” information in evaluating whether there is a high likelihood of timely biosimilar launch.

⁶² *Id.* § 1192(f)(1)(B)(ii)(III).

⁶³ *Id.* § 1192(f)(1)(B)(ii)(I)(bb).

⁶⁴ Scalia & B. Garner, *Reading law: The interpretation of legal texts* 199, 203-132-33 (2012).

Congress could not have intended such a perverse result, especially when it renders part of the statutory text in subclause (aa) completely nugatory. The only way to give meaning to the entirety of section 1192(f) is to understand that section 1192(f)(3) does not set forth the only set of information and documents that CMS may consider. CMS may consider **all** information and documents submitted in rendering its determination.

Of note, such an approach also makes logical sense in light of the broader context of the biosimilar delay provision. As noted above in Section III(C)(3), there is a wide range of information that informs whether there is a high likelihood that a biosimilar will be timely marketed. There is no one-size-fits-all approach to identifying the types of information that will help CMS determine whether to grant any particular request for a delay. Congress could not have intended for CMS to render a decision without considering information that is necessary to doing so. As biosimilar manufacturers are in the best position to determine what information may be relevant to that determination, CMS should request and consider all information deemed by a biosimilar manufacturer to support a high likelihood determination.⁶⁵

4. CMS Should Clarify What Circumstances Constitute an Agreement That Incentivizes a Biosimilar Manufacturer to Request a Delay

CMS is not permitted to grant a request for a delay where, based on specified information, the biosimilar manufacturer and reference biologic manufacturer have entered into an agreement that requires or incentivizes the biosimilar manufacturer to submit a delay request.⁶⁶

We appreciate the Guidance's confirmation that agreements between reference biologic manufacturers and biosimilar manufacturers, particularly those that enable a biosimilar manufacturer to market a biosimilar, are **not inherently disqualifying**, a conclusion that is required by the statute. Specifically, CMS implicitly but correctly acknowledges that an "agreement with the reference product manufacturing that permits the biosimilar manufacturer to market the Biosimilar in one or more dosage form(s), strength(s), and indication(s)" does not necessarily incentivize the biosimilar manufacturer to request the delay; to the contrary, CMS considers such an agreement a form of clear and convincing evidence of high likelihood that the biosimilar will timely enter the market.⁶⁷

Lilly concurs with CMS's recognition that not all agreements between reference biologic and biosimilar manufacturers incentivize a biosimilar manufacturer to request a delay. Lilly also emphasizes that any contrary interpretation would contradict the statute, which expressly provides that agreements between a biosimilar manufacturer and a reference biologic manufacturer are to be used as **evidence supporting** the likelihood that the biosimilar will come to market within the specified period, rather than treating the existence of such an agreement as categorically disqualifying.⁶⁸

While Lilly appreciates CMS's acknowledgement that the agency shares this interpretation, we also request clarification on the **specific circumstances** under which an agreement will be considered by CMS to incentivize a biosimilar manufacturer to request a delay. The only elaboration provided in

⁶⁵ As discussed in Section VI(C), confidential commercial information submitted by a manufacturer should be robustly protected from disclosure.

⁶⁶ SSA § 1192(f)(2)(C)(iv)(II)(aa).

⁶⁷ Guidance at 19.

⁶⁸ SSA § 1192(f)(1)(B)(ii)(I)(bb), (2)(B)(i)(II), (3)(B).

the Guidance is that an agreement must not “impos[e] improper constraints on the Biosimilar Manufacturer.”⁶⁹ Further elaboration is necessary particularly because biosimilar manufacturers will be required to certify that they have not entered into a disqualifying agreement (i.e., one with improper constraints), on penalty of “liability, including under the False Claims Act.”⁷⁰

Clarification of the applicable standard for identifying “improper” agreements, including examples, is needed to allow manufacturers to better understand the full range of circumstances where the agency will deem an agreement to create incentives for a biosimilar manufacturer to request a delay. Absent such clarification, the “improper constraints” standard is woefully ambiguous, especially given the significant consequences that follow if CMS finds that a disqualifying agreement exists. Manufacturers need clearer standards to be able to make informed decisions about the terms of agreements into which to enter. Greater certainty about what agreements CMS will consider improper is needed. Importantly, such clarity will facilitate agreements that **promote** biosimilar market entry, and thus further the biosimilar market competition Congress sought to promote in enacting the Program.

IV. CMS Must Rescind Its Bona Fide Marketing Standard; CMS Should Instead Use the “Market Date” Reported Under the MDRP

The statute uses the date on which a generic or biosimilar was “marketed” as a key reference point across multiple aspects of the Program’s implementation:

- **A drug or biologic is not MFP-eligible if a generic or biosimilar is marketed by what would otherwise be the drug or biologic’s selection date.** The statute specifically excludes from the definition of a “qualifying single source drug” any product that is “the listed drug for any drug that is approved and marketed under [the FDCA]” or “the reference product for any biological product that is licensed and marketed under [the PHSA].”⁷¹
- **If a biosimilar manufacturer requests and is granted a delay in the selection of a biologic for negotiation and the biosimilar is marketed within two years of the date on which the biologic would otherwise have been selected for the MFP process, the biologic will never be subject to selection for the MFP process.** Under specified circumstances, a biosimilar manufacturer will be granted a delay in selection of a biologic for negotiation “if [CMS] determines that there is a high likelihood . . . that a biosimilar biological product . . . will be licensed and marketed . . . before the date that is 2 years after [what would otherwise have been the biologic’s selection date].”⁷²
- **A biologic is not eligible for delay in selection for the MFP process if it is not marketed within one year of licensure of the biosimilar.** Specifically, the statute states that “[i]n no case shall the Secretary delay the inclusion of a biological product on the [selected drug list]

⁶⁹ Guidance at 19.

⁷⁰ *Id.* at 77, 80.

⁷¹ SSA § 1192(e)(1)(A)(iii); (B)(iii). Note that these and other provisions of the SSA refer to when a drug or biologic is **both** approved or licensed **and** marketed. The discussion herein presumes that a drug or biologic will be marketed only if it has been approved or licensed, so focuses only on the later of the two relevant dates, i.e., the date on which the drug or biologic is marketed.

⁷² *Id.* § 1192(f)(1)(A).

if more than 1 year has elapsed since the biosimilar biological product has been licensed” and “marketing has not commenced for such biosimilar biological product.”⁷³

The date on which **CMS determines** that a generic or biosimilar has been marketed also has critical implications for whether a drug or biologic will be subject to an MFP and for how long, as well as for how long a manufacturer will be assessed an excise tax if found to be non-compliant with program requirements:

- **If CMS determines after a drug or biologic is selected for the MFP process, but before the end of the “negotiation” period, that a generic or biosimilar has been marketed, the process for setting an MFP terminates.** Under the statute, a drug or biologic that has been selected for the MFP process and for which CMS has made a determination by the end of the “negotiation” period that a generic or biosimilar drug has been marketed shall not be subject to the MFP process for such period.⁷⁴
- **If CMS determines after the end of the “negotiation” period that a generic or biosimilar has been marketed, the drug or biologic generally will cease to be subject to the MFP starting with the first year that begins at least nine months after the date of such determination.** By statute, a selected drug generally will be subject to the MFP until the year that is “at least 9 months after the date on which [CMS] determines” that at least one generic or biosimilar has been marketed.⁷⁵
- **For a manufacturer that is subject to an excise tax as a result of noncompliance with program requirements, the excise tax ceases on the date on which CMS determines that a generic or biosimilar has launched.** Manufacturers may be subject an excise tax for failure to enter into an agreement to negotiate, failure to agree to an MFP, or failure to submit certain data to CMS.⁷⁶ The excise tax will cease to apply at any of certain points in time specified by statute, one of which is the date on which CMS determines that a generic or biosimilar has been marketed.⁷⁷

In the Guidance, CMS defines “marketed” in a manner that contorts this entirely straightforward statutory standard into a standard that is utterly untethered from the statute and that blatantly purports to expand agency authority far beyond the limits that Congress clearly imposed. CMS states, without any claim of statutory support, that a finding that a generic or biosimilar is “marketed” requires a finding that the generic or biosimilar presents “bona fide” competition based on the evaluation of prescription drug event (PDE) data over a 12-month period.⁷⁸ At least in the context of evaluating whether the application of the MFP should terminate, CMS states that such standard is met by reference to whether the generic or biosimilar presents “robust and meaningful competition,” as determined based on the agency’s subjective judgment.⁷⁹

⁷³ *Id.* § 1192(f)(2)(D)(iii).

⁷⁴ *Id.* § 1192(c)(2).

⁷⁵ *Id.* § 1192(c)(1).

⁷⁶ IRC § 5000D(b)(1)-(3).

⁷⁷ *Id.* § 5000D(b)(1)(B).

⁷⁸ Guidance at 62.

⁷⁹ *Id.* at 67. Note that the Guidance does not make clear if the agency intends to apply its bona fide marketing standard in all situations under the statute where the marketing of a generic or biosimilar is consequential, e.g., the biosimilar delay provision. If CMS intends to use an alternative standard in any given situation, it should clearly articulate such alternative and subject it to public comment.

For the reasons stated below, Lilly urges CMS to rescind its bona fide marketing standard as extra-statutory and therefore unlawful. CMS should instead uniformly define (1) the date on which a generic or biosimilar is marketed and (2) the date on which CMS determines that a generic or biosimilar has been marketed by reference to the MDRP market date.

A. CMS's Bona Fide Marketing Standard Is Unlawful

Lilly is deeply troubled by CMS's bona fide marketing standard for multiple reasons. First and foremost, the standard is incompatible with the clear statutory language. As a matter of plain language definitions, "marketing" refers to the "work of advertising and offering goods or services for sale,"⁸⁰ or the action of "buying or selling" in a commercial marketplace.⁸¹ This means that, once the act of selling or buying has occurred, a product necessarily **has** been marketed. CMS has no discretion to interpret the statute otherwise.

CMS has recognized as much in its very own proposed policy implementing a different provision of the IRA, which looks to how CMS has already defined the term "marketed" in analogous contexts. Specifically, as recently as February of this year, CMS proposed to determine when a drug is "marketed" for purposes of the IRA's Part D inflation rebate provision by reference to the "market date" that the manufacturer is required to report under the MDRP program.⁸² This fully accords with the fact that CMS has long defined "marketed" under the NDRA to mean that a "drug is **available for sale** by a manufacturer in the states."⁸³ And, notably, under the Part D program, CMS has long recognized that the date on which a product is "**release[d] onto the market**" triggers Part D coverage decision-making.⁸⁴ Therefore, the PDE data on which CMS's bona fide marketing standard relies to determine whether a product is "marketed" show utilization of the product **after** the point in time when the product has been recognized as having come to market – under CMS's own policy.

Simply put, CMS has already defined when a drug is "marketed," under the IRA as well as under other drug pricing programs, and none of those definitions reflects the "bona fide marketing" standard CMS has invented. Here, CMS seeks to wholly replace the statutory reference point – the date of **marketing** – with an extra-statutory standard tied to the **degree of utilization**. Doing so patently lacks any legal basis. For purposes of evaluating whether a product is marketed, it is completely irrelevant whether the product is being utilized sufficiently, particularly where sufficiency is based on the agency's subjective judgment of whether adequate competition exists. The only consideration

⁸⁰ Cambridge English Dictionary, Definition of Marketing, <https://dictionary.cambridge.org/us/dictionary/english/marketing>.

⁸¹ Oxford English Dictionary, Definition of Marketing, <https://www.oed.com/view/Entry/114186?rskey=iyHQfr&result=2#eid>.

⁸² CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1860D-14B of SSA, and Solicitation of Comments, § 40.3 (Feb. 9, 2023). The CMS proposed guidance for the Part B inflation rebate uses the "date of first sale" reported for ASP purposes, which likewise has no qualitative component in its determination. CMS, Medicare Part B Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1847A(i) of the Social Security Act, and Solicitation of Comments, § 50.3 (Feb. 9, 2023).

⁸³ NDRA § I(l); 83 Fed. Reg. 12,770 (Mar. 23, 2018) (emphasis added).

⁸⁴ CMS requires that Part D plan sponsor P&T committees "make a reasonable effort to review a new FDA approved drug product (or new FDA approved indication) within 90 days of its release onto the market and . . . make a decision on each new FDA approved drug product (or new FDA approved indication) within 180 days of its release onto the market, or a clinical justification will be provided if this timeframe is not met." Prescription Drug Benefit Manual, ch. 6 § 30.1.5.

bearing on the statutory standard of marketing is whether the **product is sold** in the commercial marketplace.⁸⁵

Second, the agency's "bona fide marketing" standard is too vaguely defined to provide notice to stakeholders of its parameters. CMS provides no concrete definition or even illuminating examples of when the agency will consider a generic or biosimilar manufacturer to have engaged in bona fide marketing. It is entirely unclear whether CMS expects the generic or biosimilar manufacturer to have captured a percentage of the market or what factors (e.g., size of market, clinical advantage offered by the reference product) CMS will consider. Even after CMS determines that the generic or biosimilar manufacturers has engaged in bona fide marketing, CMS intends to monitor PDE data for continued "robust and meaningful competition."⁸⁶ Again, CMS fails to offer any explanation of what it will look for, e.g., does the agency expect the level of competition to stay the same? To increase? The Guidance is entirely too ambiguous to put either listed drug or reference product manufacturers or generic/biosimilar manufacturers on notice of how the agency intends to operationalize the standard.

Third, this very subjectivity provides CMS with boundless authority that Congress clearly did not delegate. The MFP termination date is a notable example. That date is defined by reference to the date on which CMS determines that a generic or biosimilar has been marketed.⁸⁷ There is a simple and straightforward means for making this determination: the MDRP market date. CMS recognizes that such date triggers the start of MDRP rebate liability as well as the IRA's Part D inflation rebate liability, but, on no justifiable basis, does not recognize that such date triggers the termination of MFP liability. CMS's bona fide marketing standard purports to vests the agency with limitless discretion to delay the MFP termination date, even indefinitely, based on the agency's subjective judgment as to the extra-statutory consideration of utilization sufficiency.

In addition, CMS is implicitly asserting the authority to **re-institute** an MFP after one has been terminated, if the agency concludes based on PDE data that utilization of the generic or biosimilar ceases to be "robust and meaningful."⁸⁸

Nothing in the text or structure of the statute purports to give CMS such sweeping authorities. Through its bona fide marketing standard, CMS is "effectively [seeking to] introduce[e] a whole new regime of regulation," which "is not the one that Congress established."⁸⁹ This is patently unlawful. "It is axiomatic that an administrative agency's power to promulgate legislative regulations is limited to the authority delegated by Congress. . . . Thus, if there is no statute conferring authority, a federal agency has none."⁹⁰

⁸⁵ Congress knows full well how to impose a "bona fide" qualitative standard when evaluating a given activity in relation to drug pricing. In the context of the MDRP, Congress specifically amended the statute to clarify that only "bona fide" service fees are exempt from the calculation of Average Manufacturer Price. SSA § 1927(k)(1)(B)(i)(II) as amended by Pub. L. 111-148, § 2503(a) (2010). And, in implementing that standard, CMS has engaged in extensive rulemaking to define the parameters of the "bona fide" determination. See 81 Fed. Reg. 5170 (Feb. 1, 2016). Such statutory basis for a "bona fide" standard is notably absent here, yet CMS is impermissibly purporting to substitute this standard for the one clearly prescribed by Congress.

⁸⁶ Guidance at 67.

⁸⁷ SSA § 1192(c)(2).

⁸⁸ See Guidance at 67.

⁸⁹ *MCI Telecomms. Corp. v. Am. Tel. & Tel. Co.*, 512 U.S. 218, 114 (1994).

⁹⁰ *Michigan v. EPA*, 268 F.3d 1075, 1081 (D.C. Cir. 2001).

Fourth, CMS's approach **guarantees** a significant delay between the date on which CMS determines that a generic or biosimilar has been marketed and the date on which the generic or biosimilar was in fact marketed. This is because it takes time for sales to be reflected in the PDE data. Under CMS's long-standing policy, Part D plan sponsors must determine within 180 days from the date on which a newly approved drug is released onto the market whether to add the drug to their formulary. Many Part D plan sponsors will not add a newly approved drug to their formulary until the 180-day mark, and, thus, the first six months of PDE data following the market entry of the drug will **necessarily** reflect only very limited uptake. The absence of PDE data, then, by no means substantiates the absence of marketing. CMS's bona fide marketing standard (exacerbated by the agency's intent to evaluate PDE data only once per month)⁹¹ clearly contradicts the statute as it ensures that CMS's determination of when a generic or biosimilar has been marketed will not accurately reflect when the generic or biosimilar was in fact marketed. Further, PDE data are not publicly available or otherwise transparent and thus, further aggravate credibility and verification concerns with the MFP process.

Compounding this concern is that, even where plan sponsors add a newly approved generic or biosimilar to their formulary, widespread utilization of the generic or biosimilar cannot be expected to occur overnight. Even after a product is made available for sale, providers and patients must become comfortable with switching to the new product.⁹² Under any rational interpretation of the word, the product is marketed during this transition period. And the fact that there may be a period of transition before claims data reflect a higher-level utilization does not mean that the market is failing to work as intended.

From a policy perspective, generic and biosimilar competition is a bedrock for affordability in the pharmaceutical industry. Approximately 90% of the drugs used in the US are generic^{93, 94} and come at significantly reduced prices (i.e., approximately 20% of the brand drug price for oral generics within the early years of generic availability)^{95, 96} Generic drug prices are so low that the environment has been described as a "race to the bottom" in terms of pricing, a situation that many have argued is unsustainable and leads to shortages, generic manufacturers leaving the market. By not being clear and setting the "marketed" bar arbitrarily and unnecessarily high for generic competition to be sufficient to remove a selected drug and allow for normal market-based competition, CMS increases the likelihood that generic drugs will be competing in the market with their reference branded drugs

⁹¹ Guidance at 62.

⁹² Uptake of a biosimilar, in particular, can be slow for myriad reasons. *See, e.g.,* Zachary Brennan, *Biopharma CEOs Explain Problems with Biosimilars to Congress*, Regulatory Aff. Profs. Soc'y (Apr. 12, 2019), available at <https://www.raps.org/news-and-articles/news-articles/2019/4/biopharma-ceos-explain-problems-with-biosimilars-t> (for example, uptake may be limited "due to physician confusion regarding interchangeability and extrapolation, and a lack of physician, patient, and payer incentives").

⁹³ Association for Accessible Medicines (2021, October 14). *The U.S. Generic & Biosimilar Medicines Savings Report*. The U.S. Generic & Biosimilar Medicines Savings Report. <https://accessiblemeds.org/sites/default/files/2021-10/AAM-2021-US-Generic-Biosimilar-Medicines-Savings-Report-web.pdf>

⁹⁴ USC Schaeffer Center (2022, May 21). *U.S. Consumers Overpay for Generic Drugs*. USC Schaeffer Center White Paper Series. <https://healthpolicy.usc.edu/research/u-s-consumers-overpay-for-generic-drugs/>

⁹⁵ US Food and Drug Administration (2021, November 1). *Generic Drug Facts*. <https://www.fda.gov/drugs/generic-drugs/generic-drug-facts>

⁹⁶ IMS Institute for Health Informatics (2016, January 1). *Price Declines after Branded Medicines Lose Exclusivity in the U.S.* <https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/price-declines-after-branded-medicines-lose-exclusivity-in-the-us.pdf>

being subject to the MFP. In this situation, the generic drug, in order to be competitive, would necessarily have to price their drug at roughly 20-40% of the MFP of the reference product, which is already deeply discounted. Given fixed costs of development and the already “race to the bottom” environment for generic manufacturers, this policy would put the sustainability of the generic industry as a whole in jeopardy and could result in monumental impacts to patient affordability in commercial (and public) markets. Combining this issue with the untenable burden on the biosimilar manufacturers to submit a delay request without knowing if the reference product of relevance is being selected, (argued elsewhere in the letter), in total, represents a lack of alignment by CMS with the IRA’s intent to safeguard the biosimilar and generic industry.

CMS should make every effort to avoid any delay in its determination that a generic or biosimilar has been marketed, as such a delay may be of enormous consequence to reference biologic manufacturers and biosimilar manufacturers alike. In particular, Lilly is concerned that the prospect of an unnecessarily extended MFP will create dramatic disincentives against generic and biosimilar market entry, thereby defeating Congress’s objective of encouraging such market-based competitors.⁹⁷

B. CMS Should Instead Set the Program Date of Marketing and the Date of CMS’s Determination of Marketing by Reference to the Definition of “Marketed” in the NDRA

A lawful and infinitely more reasonable approach would be for CMS to define the date of marketing and the date of CMS’s determination of marketing in a uniform fashion by reference to the familiar market date already reported by manufacturers for purposes of the MDRP.

Specifically, CMS defines “market date” in MDRP guidance as “the earliest date the drug was first marketed under the application number by any labeler.”⁹⁸ The NDRA in turn provides that a drug is first “marketed” on the date on which it was first “**available for sale** by a manufacturer in the states.”⁹⁹

Manufacturers routinely report this date when reporting pricing data under the MDRP, and such date is ascertainable for generics and biosimilars regardless of whether they are subject to ASP reporting.¹⁰⁰ Thus, there exists a long-standing construct with which CMS and manufacturers are well familiar, and to which they have ready access, on which the agency can and should rely to determine the date on which a generic or biosimilar launched for purposes of the Program. This approach has the added benefit of ensuring consistency across the MDRP and the Program for both the agency and manufacturers.

Adoption of the NDRA definition of “marketed” for purposes of the Program would eliminate any legal concerns, as CMS would be adopting a standard that comports with the plain language definition of marketing. Lilly emphasizes that it is especially critical that this standard be adopted in the context of the date of **CMS’s determination** of the date of marketing: As noted above, if there is a lag of even

⁹⁷ In addition, a lag of a single day between the date of marketing and the date of CMS’s determination of such marketing can result in the MFP being extended for a full additional year.

⁹⁸ CMS, MDRP Data Guide § 5.15 (Apr. 2022).

⁹⁹ NDRA § I(l); 83 Fed. Reg. 12,770 (Mar. 23, 2018) (emphasis added).

¹⁰⁰ The “first sale date” reported for ASP purposes is not a reliable method for determining the date of marketing here. The date of first sale is reported only for products subject to ASP reporting, and thus may not be available for all generics and biosimilars whose marketing is implicated by the Program, whereas the market date reported under the MDRP is more broadly reported and therefore a better metric to use.

one day between the date of marketing the date of CMS's determination of such marketing, a selected drug can be subject to the MFP for **an additional 12 months**.

V. Pre-Selection Process

- A. *CMS Should Notify a Manufacturer of Any Drug That the Agency Intends to Select for the MFP Process in Advance of the Selection Date and Afford Such Manufacturer a Reasonable Opportunity to Dispute the Propriety of the Intended Selection*

CMS should implement a “pre-selection” process whereby a manufacturer of a drug intended to be selected for the MFP process is notified of such intended selection and permitted to identify any concern to the agency in advance of the selection date. This process will enhance informed decision-making and promote efficiency and transparency.

As CMS knows, there is an inherent risk of error in the process of selecting drugs for the MFP process given the complexity of the statutory process. Eligibility is based on a myriad of factors, including whether a sufficient number of years post-approval or licensure have passed;¹⁰¹ whether a generic or biosimilar is marketed;¹⁰² whether an exclusion applies, for plasma-derived products, low Medicare spend drugs, certain orphan drugs, and small biotech drugs;¹⁰³ and whether Medicare expenditures are sufficiently high to qualify the drug for eligibility for selection.¹⁰⁴

As such, it is important that there be a mechanism to avoid erroneous selections. Further, it is critical that such mechanism be available in **advance** of the selection date – because, if an error in selection is identified **after** the selected drug publication date, the erroneously selected drug would be de-selected, but **no alternative** could be substituted. This is because the statute **requires** CMS to publish a list of drugs selected for the MFP process by no later than February 1 of the year that is two years before the applicable IPAY (or September 1, 2023, for IPAY 2026).¹⁰⁵

A pre-selection process will therefore both reduce the risk of error **and** facilitate a complete list of selected drugs. To make such pre-selection process meaningful, Lilly also recommends that CMS provide notice to affected manufacturers at least 30 days in advance of the selection date and afford manufacturers at least 14 days thereafter to respond to the agency with concerns.

In addition, CMS should include as part of the pre-selection process at least the next five drugs that would be selected as a substitute if, through the pre-selection process, CMS determines that a drug intended to be selected is, in fact, ineligible. This would enable manufacturers of such drugs to engage with the agency to similarly ensure that any such drug would be appropriate for substitution. This added process is particularly reasonable because there is no additional burden on the agency associated with identifying these additional drugs, given that CMS will already have identified the 50 qualifying single source drugs with the highest total Part D expenditures and, starting with IPAY 2028, the top 50 qualifying single source drugs with the highest total Part B expenditures.¹⁰⁶

¹⁰¹ *Id.* § 1192(e)(1).

¹⁰² *Id.*

¹⁰³ *Id.* §§ 1192(e)(3)(A)–(C), 1192(d)(2).

¹⁰⁴ *Id.* § 1192(d)(1)

¹⁰⁵ *Id.* § 1191(b)(3), (d)(1).

¹⁰⁶ *See id.* § 1192(d)(1).

B. CMS Should Also Establish a Pathway Whereby Biosimilar Manufacturers Can Solicit Information Regarding Whether CMS Intends to Select the Applicable Reference Biologic in Advance of the Deadline for Submitting a Biosimilar Delay Request

CMS should foster market-based price competition by creating a reasonable process by which biosimilar manufacturers can solicit information from CMS necessary to determine whether such manufacturers should submit a delay request under the statute.

The statute allows a biosimilar manufacturer to request a delay of the selection of a reference biologic for the MFP process where there is a high likelihood that a biosimilar for that biologic will be licensed and marketed within two years of what would otherwise have been the reference biologic's selection date, **so long as** the request is made **before** the reference biologic's selection date.¹⁰⁷

This timing requirement creates a dilemma for biosimilar manufacturers: A biosimilar manufacturer cannot determine whether it should request a delay without knowing whether an applicable reference biologic will be selected for the MFP process for a given year. But, in the ordinary course, the biosimilar manufacturer will have knowledge of the reference biologic's selection only **after** the selection date passes and the list of selected drugs is published, at which point it will be too late to request a delay. CMS acknowledges this conundrum in the Guidance, but the only advice it provides is that manufacturers should look to publicly available data and submit a delay request if they "**think** that a Reference Drug for their Biosimilar **may** be a selected drug."¹⁰⁸

It is patently unreasonable and inefficient for CMS to require biosimilar manufacturers to expend significant time and resources on biosimilar delay requests simply because a reference biologic "may" be subject to selection. Further, expecting biosimilar manufacturers blindly to guess as to whether to submit a delay request risks subverting Congress's purpose in creating the delay request process. Many biosimilar manufacturers may fail to submit such requests, simply because they are not aware that there is a serious risk that a reference biologic is a likely candidate for selection. This risks undermining the very purpose of Congress in creating the biosimilar delay request process, which is to incentivize market competition by encouraging the development of biosimilars by providing a longer runway of time for such development.

Rather than perpetuating unnecessary roadblocks to timely biosimilar delay requests, CMS should establish a process that makes the delay request process as meaningful as possible. The most logical and straightforward means of doing so is simply to allow biosimilar manufacturers to inquire with CMS whether an applicable reference biologic is anticipated for selection in advance of the delay request submission deadline. CMS should permit biosimilar manufacturers to solicit such information starting at least 30 days in advance of the biosimilar delay request deadline to ensure they have adequate time to make an informed decision regarding whether to request a delay.

VI. The MFP "Negotiation" Process

A. CMS Should Enhance the Proposed "Consistent Methodology and Process" for Initially Setting the MFP ("Negotiation") and Resetting the MFP ("Renegotiation")

The statute provides that CMS must "develop and use a consistent methodology and process" to

¹⁰⁷ *Id.* § 1192(f)(1)(B)(i)(2), 1192(f)(1)(A).

¹⁰⁸ Guidance at 16-17 (emphasis added).

negotiate the MFP.¹⁰⁹ Additionally, the statute provides that, beginning in 2028, CMS may enter into renegotiations for a selected drug in certain circumstances specified by statute, and that CMS must “specify the process for renegotiation,” which “shall, to the extent practicable, be consistent with the methodology and process” for initial negotiations.¹¹⁰ Thus, Congress intended the methodology and process governing both negotiation and renegotiation to be transparent and predictable for all entities involved.

Under the Guidance, CMS lays out its proposed framework for how the MFP process will proceed, including the process governing CMS offers, manufacturer counteroffers, and CMS responses to counteroffers – including justifications supporting such offers, counteroffers, and responses. CMS also proposes a framework for meetings between the manufacturer of the selected drug and the agency. Under the Guidance, such meetings will occur only where CMS rejects a manufacturer counteroffer, in which case CMS will extend a meeting invitation.¹¹¹ The initial meeting is to take place within 30 days of receipt of the counteroffer. Thereafter, CMS proposes to allow each party the opportunity to request one additional meeting – such that a maximum of three meetings is possible for each selected drug.¹¹² At such meetings, the parties may discuss new information bearing on the negotiation of the MFP.¹¹³

Lilly asks that CMS modify its proposed MFP process to include the recommendations set forth below.

1. CMS Should Commit to Engaging in Bespoke Negotiations with Each Manufacturer of a Selected Drug

CMS’s proposal allows for potential dialogue between the parties, which represents an important step toward implementing a meaningful process “for negotiations” as part of the Program.¹¹⁴ Nevertheless, we are concerned by the arbitrary limitations on engagement in the Guidance. As noted above, under the Guidance, real dialogue is limited to (1) instances where CMS rejects a counteroffer and (2) a maximum of three meetings. Importantly, the benefit of meaningful dialogue is not limited to when a counteroffer has been rejected. Engagement between the parties is equally beneficial in informing an initial offer. In fact, such early discussions can negate the need for a counteroffer, thereby generating efficiencies for both the agency and manufacturers.

Even more concerning is the arbitrary cap on the number of allowable meetings. Lilly does not see any benefit to establishing a categorical limit on the number of meetings between the parties. If both CMS and the manufacturer of the selected drug believe that one or more additional meetings would be productive to setting a more appropriate MFP, then CMS should allow such additional meetings to proceed rather than cutting off helpful discussions prematurely based on an arbitrary limit on the total number of meetings permitted.

Lilly recommends that CMS modify its proposed MFP setting process to allow for greater dialogue between the parties throughout the process and to specify that additional meetings (beyond the current maximum of three) may be held if agreed to by both parties. Further, to ensure productive dialogue, we urge CMS to commit to engaging substantively with the manufacturer in each meeting.

¹⁰⁹ SSA § 1194(b)(1).

¹¹⁰ *Id.* §§ 1194(f)(2), (4)(A)-(B).

¹¹¹ Guidance at 55.

¹¹² *Id.* at 55–56.

¹¹³ *Id.* at 56.

¹¹⁴ SSA § 1194(b)(1).

Given the limited number of drugs subject to negotiation in a given year, the recommended changes are manageable for the agency to implement and will facilitate a more productive and tailored process – which will be critical to any success under the program. There is also ample time to effectuate any additional meetings. The statute requires CMS to make the initial offer by June 1 of the year of the selection year (February 1, 2024, for IPAY 2026) and also provides that the manufacturer must accept the offer or make a counteroffer within 30 days.¹¹⁵ Even if CMS were to wait until June 1 (February 1 for IPAY 2026) to make the initial offer, and even if the manufacturer were to wait until the 30th day to make a counteroffer, there would still be four remaining months in the negotiation period (five for IPAY 2026). Therefore, more than adequate time exists in the negotiation timeline for the contemplated additional process.

2. CMS Should Commit to Considering All Information Submitted by a Manufacturer in Setting the MFP

CMS should specify that it will consider **all** information submitted by manufacturers throughout the process. Although the justifications for the initial offer and the manufacturer's counteroffer are moored to the negotiation factors enumerated in the statute, the statute by no means precludes CMS from considering additional information that a manufacturer determines relevant to the MFP process.¹¹⁶ Further, CMS's counteroffer responses are not statutorily required to be justified by reference to the statutorily enumerated negotiation factors.¹¹⁷ The statute clearly permits the agency to set the MFP by reference to any and all information submitted by manufacturers, and CMS should commit to considering all such information.

In the Guidance, CMS does not specify that a manufacturer may submit, and that the agency will consider, any information that the manufacturer determines relevant to the MFP process. The accompanying proposed information collection request (ICR) suggests that this is intentional, as the proposed ICR solicits information **only** with respect to the statutorily enumerated negotiation factors (and, even then, does so in an unduly cramped manner by imposing a severe word limit) and does **not** provide for any supplementary submission.¹¹⁸ CMS should not narrow the universe of relevant evidence that it will consider during the MFP setting process.

3. CMS Should Fulsomely Justify the Initial Offer and Any Response to a Counteroffer in Writing and Afford Manufacturers an Opportunity to Comment on Any Response Before an MFP Is Set

It is important that CMS provide a meaningful justification in support of its offers and responses to any counteroffers. Negotiations involving offers and counteroffers are commonplace in the commercial sector. And they commonly entail robust, open, and bilateral dialogue between the parties to facilitate mutually agreeable terms. By establishing a “negotiation” process, Congress intended the Program to be premised on such familiar concept.

Congress also established requirements to facilitate transparency in the process, which is a necessary

¹¹⁵ SSA § 1191(d)(5)(B), 1194(b)(2)(B).

¹¹⁶ See *id.* § 1194(b)(2)(B), (C)(ii)(II).

¹¹⁷ *Id.* § 1194(b)(2)(D).

¹¹⁸ CMS, Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (CMS-10847, OMB 0938-NEW) (ICR Form for Negotiation Data Elements).

predicate to good faith dialogue during negotiations. By statute, CMS must provide an initial offer, in writing, to the manufacturer of the selected drug and include with it a justification based on the factors described in section 1194(e) of the SSA.¹¹⁹ The manufacturer of the selected drug may make a counteroffer to the initial offer, and, where the manufacturer does so, CMS must respond in writing.¹²⁰

These statutory requirements limit the scope of the agency's discretion under the statute, and such limitation can be meaningfully effectuated only if CMS is fully transparent as to the information under section 1194(e)(2) on which the agency relied. Additionally, to abide by the patient-centered intent of this statutory program, CMS must describe what threshold and measurement will be used to "determine the effects of the selected drug and its therapeutic alternative(s) on specific populations"¹²¹ and whether the selected drug fills an "unmet medical need."¹²² It is well known that patient centricity has revealed a misalignment between what patients report as important to them about their disease and/or treatment, and the data and measurements typically utilized in research and public policy decision-making.¹²³ If CMS relies more heavily on "Manufacturer-Specific Data" (section 1194(e)(1)) than "Evidence About Alternative Treatments" (section 1194(e)(2)), including data supporting "unmet medical need," CMS may be disregarding what is most meaningful to patients.

When determining therapeutic alternatives for a selected drug, CMS should rely on external organizations for purposes of evidence synthesis or technology assessment only if such organizations meet specified standards. Such standards should ensure organizational independence, patient-centered procedures and methods, methodological rigor, and transparency. CMS should apply these same rigor and transparency standards to its internal "claims analysis" and review when adjusting the MFP starting point based on clinical evidence.¹²⁴ Furthermore, we recommend that the MFP for a selected drug be set at the ceiling if such drug demonstrates significant patient benefit.

To give meaning to the agency's stated goal of promoting transparency, we urge CMS to commit to including meaningful explanations as to how the agency arrived at the offer and the response to any counteroffer, including how the offer or response is supported by statutorily enumerated negotiation factors, how such factors (and any other information) were weighed and considered, and any non-manufacturer sources of information relied upon.¹²⁵

Additionally, we ask that CMS agree to respond to any counteroffer within 30 days of receipt. We also ask that CMS agree to give manufacturers at least 30 days to comment on the response. For any such comment process to facilitate a more effective MFP process, CMS must actually consider the comments before setting the MFP. We ask CMS to commit to this. Not only will this further transparency and fairness in the MFP process, but it will also help to ensure that the agency is not inadvertently setting the MFP based on any misunderstanding or gap in information.

¹¹⁹ *Id.* §§ 1191(d)(5)(B), 1194(b)(2)(B).

¹²⁰ *Id.* § 1194(b)(2)(C)–(D).

¹²¹ *Id.* § 1194(e)(2)(C).

¹²² Guidance at 60.3.3.1.

¹²³ Perfetto, E.M., Oehrlein, E.M., Love, T.R., Bright, J., & A. Kennedy. "Patient-Centered Core Impact Sets: What They Are and Why We Need Them." *The Patient – Patient-Centered Outcomes Research* (2022).

¹²⁴ Guidance at 60.3.3.

¹²⁵ See CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026 (Jan. 11, 2023).

4. CMS Should Clarify That a Manufacturer May Broadly Supplement Its Timely Submission After the Submission Deadline Where Subsequent Developments Arise or Otherwise for Good Cause

As part of the MFP process, a manufacturer of a selected drug will be required to submit certain information regarding the drug's non-FAMP, as well as other specified information relevant to the MFP process.¹²⁶ For example, the statute contemplates the manufacturer submitting data regarding research and development costs, production and distribution costs, market data, and revenue and sales volumes.¹²⁷ Further, CMS has signaled that the manufacturer will be permitted to submit evidence about alternative treatments.¹²⁸

Such manufacturer-provided information must be submitted by March 1 of the year of the selection date (or October 2, 2023, for initial price applicability year (IPAY) 2026), just one month after a drug is selected for negotiation.¹²⁹ Given this tight deadline, there is a very real possibility that unforeseeable changes will occur after the submission deadline, such as new data regarding comparative effectiveness becoming available, a new therapeutic alternative coming to market, production costs unexpectedly increasing, or restatement of pricing data.

Manufacturers have every incentive to diligently comply with CMS's submission requirements, but there is a legitimate need for flexibility in allowing manufacturers to supplement their timely submissions to ensure CMS has the most accurate understanding of the dynamics surrounding the selected drug. This is especially so both because of the novelty of the program and in light of the fact that manufacturers have only a month to compile and submit voluminous amounts of complex information. In some cases, the required information may not even be available in the format that CMS requests at the time of an initial submission.

The agency's current proposal does acknowledge that there may be a need to provide supplemental information to the agency after the submission deadline, but inexplicably limits presentation of such new information to **the negotiation meetings**. This is inadequate. As CMS knows, new information can take many forms, including detailed new empirical evidence, records of governmental action, and other materials not amenable to being provided or meaningfully digested in the context of a meeting discussion. And limiting the presentation of such information to the negotiation meetings necessarily means that CMS will be unable to review and consider that information ahead of such meetings, making those meetings less efficient than they otherwise could be. Moreover, such meetings will occur only where there is a rejection of a manufacturer offer, such that there is no vehicle for consideration of new information at the initial offer stage, rendering the MFP process unnecessarily inefficient.

Given the very short period afforded for preparation of an initial submission and the real possibility that new information of relevance to the MFP setting process will become available after the submission deadline, we ask that CMS to establish a more meaningful process to share additional

¹²⁶ *Id.* §§ 1194(b)(2)(A), 1193(a)(4). Presumably, CMS will designate information submitted by manufacturers under section 1194(e)(1) as information that is due by March 1 of a given year (or October 2, 2023, for IPAY 2026) under section 1193(a)(4).

¹²⁷ *Id.* § 1194(e)(1).

¹²⁸ CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026, at 2 (Jan. 11, 2023), available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf>; see also SSA § 1194(e)(2).

¹³⁰ SSA § 1194(e)(1).

information with the agency after the submission deadline has passed. Specifically, **in addition to being able to share new information at negotiation meetings**, CMS should broadly permit a manufacturer to supplement a timely submission if new information of relevance to the MFP process becomes available after the submission deadline or otherwise for good cause shown.

B. CMS Should Permit Manufacturers to Rely on Reasonable Assumptions in Connection with Information Submissions and Provide Voluntary Explanations of Information Submissions As Appropriate

Under the Program, manufacturers must submit vast quantities of information to CMS, and the agency must then consider such information, along with certain other statutorily enumerated negotiation factors. Required manufacturer-submitted information includes research and development costs of the selected drug, current unit costs of production and distribution of the drug; prior federal financial support for certain discovery and development of the drug; data on certain pending and approved patent applications, FDA exclusivities, and FDA applications or approvals regarding the drug; and market, revenue, and sales volume data in the United States for the drug.¹³⁰ CMS appears to intend such information to be submitted only through its proposed ICR.¹³¹

1. CMS Should Revise Its Proposed ICR to Allow Manufacturers Greater Ability to Provide Voluntary Explanations of Information Submissions

Consistent with the agency's own recognition of the importance of assumptions with respect to research and development costs and current unit costs of production and distribution,¹³² CMS should apply such reasoning to all other data elements. The proposed ICR includes fields for manufacturers to provide voluntary explanations of the data submitted.¹³³ However, the fields are limited to explanations of how a manufacturer made a particular calculation and are subject to word limits.¹³⁴

Lilly is concerned that the proposed ICR provides manufacturers no meaningful way to justify or provide additional background and context with respect to their data submissions, beyond that which is specifically requested by CMS in the accompanying instructions. It is vital that CMS provide manufacturers the opportunity to do so, as it will provide CMS with meaningful insight into how manufacturers developed their submissions and any assumptions the manufacturer was required to make in seeking to fulfill its data submission obligations. Our recommendation is consistent with the agency's framing of such fields in the Guidance as space for "narrative text."¹³⁵

This recommendation is especially critical with respect to products approved long ago as the information required to complete a data field may be unavailable due to common data retention policies or otherwise in the course of business. Under these circumstances, CMS must afford manufacturers flexibility to comply with information requests – for example, with respect to research and development expenses, by allowing manufacturers to stipulate to the fact that direct costs were recouped in the explanation section.

¹³⁰ SSA § 1194(e)(1).

¹³¹ See ICR for Negotiation Data Elements.

¹³² Guidance at 53.

¹³³ ICR Form for Negotiation Data Elements.

¹³⁴ *Id.*

¹³⁵ Guidance at 53.

For these reasons, we recommend that CMS specify that manufacturers may include voluntary explanations as part of their data submissions, and that the agency commit to considering such explanations. To allow for submission of any such explanations as appropriate, CMS should remove the arbitrary word limit. The ability to justify data submissions is of the utmost consequence when potentially hundreds of millions of dollars in CMPs are on the line should CMS believe that a submission of required information is false or incomplete.

We further urge CMS to permit manufacturers to stipulate to the fact that they have “recouped” their direct research and development (R&D) costs on a particular product should they so choose. As noted above, several drugs that CMS may consider for inclusion on the list of drugs subject to price setting were approved decades ago. Routine document retention, retirement, and destruction policies will likely render collecting the data necessary to precisely report direct R&D expenditures for such products impossible. Moreover, it does not matter – for innovative biopharmaceutical manufacturers – whether R&D costs have been “recouped.” Discovering new chemical or biological entities is not like “discovering” the next generation of the iPhone or building a utility, for example. Where there is relative certainty that a new product will “work,” a recoupment calculation might make sense. For biopharmaceuticals, discovery is high risk, and successfully launching a product is far from assured. Revenue from currently marketed products fund the exploration, research, and discovery of future medicines. Characterization of the goal as “recoupment” is wrong – finding the next cure, or the next dozen cures, is what we do. Consequently, whether CMS determines that a product has “recouped” its own R&D costs is, frankly, not the reference point.

2. CMS Should Permit Manufacturers to Rely on Reasonable Assumptions

In addition, CMS should specify that manufacturers may make reasonable assumptions when interpreting statutory (or any future regulatory) requirements regarding such information submissions.¹³⁶ As CMS well knows, reasonable assumptions serve an important role to bridge gaps in statutory, regulatory, and sub-regulatory instructions. There are often unresolved ambiguities in how complex information submission requirements interact with equally multi-faceted business practices and products. Reasonable assumptions allow manufacturers to set forth their understanding of how legal requirements apply to their singular circumstances, and thereby help to ensure that regulatory regimes can be operationalized even where significant ambiguities cannot reasonably be expected to be clarified or resolved, particularly on a regulated entity-by-regulated entity basis.

CMS also already has well-established frameworks governing reasonable assumptions. For example, in the ASP and MDRP reporting contexts, CMS has long permitted manufacturers to make reasonable assumptions where there is no agency guidance addressing a given issue.¹³⁷ CMS can and should readily adopt a similar approach here. In doing so, manufacturers will be permitted to make reasonable assumptions in furnishing required information consistent with the general requirements and intent of the Program, applicable regulations, and customary business practices. As noted above, such reasonable assumptions can be documented and described in the proposed ICR, such that the agency is apprised of manufacturers’ thinking and assumptions.

Neither the Guidance nor the proposed ICR addresses reasonable assumptions. Rather, the Guidance

¹³⁶ See SSA § 1194(e)(1); see also *id.* §§ 1193(a)(4), 1194(b)(2)(A) (manufacturer information submission obligations).

¹³⁷ See, e.g., 71 Fed. Reg. 69,624, 69,667 (Dec. 1, 2006) (reasonable assumptions regarding ASP reporting); 83 Fed. Reg. 12,770, 12,785 (Mar. 23, 2018) (MDRP agreement provision governing reasonable assumptions).

sets forth an appendix of proposed definitions related to manufacturer-specific data,¹³⁸ and the proposed ICR restates the proposed definitions.¹³⁹ This approach is problematic – because the agency proposes a standardized and rigid data submission framework applicable to all manufacturers and products.

Such a framework will inevitably lack the flexibility needed to accommodate the unique attributes that necessarily characterize the multitude of therapies eligible for selection for the MFP process. For context, there are over 20,000 prescription drug products currently approved for marketing in the United States, each with its own unique attributes.¹⁴⁰ Among other things, there are myriad differences in products' development histories, FDA regulatory histories, chains of ownership, and pricing and sales arrangements across the multi-layered drug distribution chain. Accordingly, it is impossible to develop a coherent “one-size-fits-all” approach to data submissions (and ill-advised for CMS to seek to do so). Attempting to shoehorn countless varying technologies, business practices, and circumstances into a single framework will inevitably result in less useful, relevant, and complete information being provided to CMS. It will also be a recipe for arbitrary decision-making.¹⁴¹ CMS will effectively be blinding itself to the full complement of data that a manufacturer deems most relevant to its product's development and pricing and that it reasonably views as falling within the categories of information required by statute to be considered.¹⁴²

As such, Lilly recommends that CMS rescind its appendix of proposed definitions (also included in the proposed ICR). CMS should instead adopt the aforementioned approach grounded in CMS's long-standing reasonable assumptions framework, and not attempt to shoehorn a broad universe of unique circumstances into highly regimented and inflexible data definitions. To the extent CMS disregards Lilly's request, please see Appendix B to this letter setting forth some of our preliminary concerns with CMS's data requests (in light of the compressed comment period and the complexity of this issue, we reserve the right to supplement this information later).

C. Confidential Commercial Information

1. CMS Should Establish More Robust Safeguards to Ensure That Confidential Commercial Information Submitted by Manufacturers Is Protected from Disclosure

The Program requires manufacturers to submit a host of information to CMS, including highly confidential manufacturer-specific data regarding research and development costs, revenue information, and sales volumes data.¹⁴³ Congress recognized the havoc that would be wreaked if sensitive information were publicly disclosed. As such, the statute imposes a stringent duty on CMS to maintain the confidentiality of such information: “Information submitted to the Secretary under this part by a manufacturer of a selected drug that is proprietary information of such manufacturer (as determined by the Secretary) shall be used only by the Secretary or disclosed to and used by the

¹³⁸ See Guidance, app. C.

¹³⁹ See ICR Form for Negotiation Data Elements.

¹⁴⁰ See FDA, Fact Sheet: FDA at a Glance, <https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance#:~:text=There%20are%20over%2020%2C000%20prescription,FDA%2Dapproved%20animal%20drug%20products> (Aug. 17, 2022).

¹⁴¹ See 5 U.S.C. § 706(2)(A).

¹⁴² See *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (agency decision-making must be based on **relevant** data and cannot fail to consider important aspects of the problem at hand).

¹⁴³ SSA § 1194(e)(1).

Comptroller General of the United States for purposes of carrying out this part.”¹⁴⁴

Consistent with this broad statutory mandate of confidentiality, CMS states in its Guidance that it intends “to implement a confidentiality policy that is consistent with existing requirements for protecting proprietary information, such as Exemption 4 of [the Freedom of Information Act (FOIA)].”¹⁴⁵ However, the Guidance is devoid of any meaningful detail as to **how** CMS specifically intends to protect the confidential and proprietary information of manufacturers.

Lilly strongly urges CMS to specify the specific safeguards that the agency will put into place to protect the confidentiality of manufacturer information, including by adopting the safeguards described below. Lilly also urges CMS to implement all such safeguards in a manner that maximizes protection of confidential commercial information. Further, Lilly emphasizes that requirements of confidentiality are meaningful only if there are consequences in the event of a breach. As such, failure by CMS to protect confidential commercial information should result in a “renegotiation” if the manufacturer requests it.

i. Scope of Protection for Confidential Commercial Information

CMS’s Guidance confirms that, at minimum, the familiar safeguards under FOIA will apply to information submitted under the Program.¹⁴⁶ Lilly appreciates this confirmation, including with respect to FOIA Exemption 4’s prohibition on disclosure of information designated as confidential without providing a pre-disclosure notification and an opportunity to raise objections to disclosure.¹⁴⁷ Lilly also requests that CMS explicitly confirm that that, under the Program, manufacturer information will also be protected from disclosure to the same extent as such information is so protected under all other applicable federal laws and policies. For example, the Medicare statute provides that information submitted by manufacturers that relates to ASP “is confidential and shall not be disclosed by [CMS] in a form which discloses the identity of a specific manufacturer . . . or prices charged for drugs or biologicals by such manufacturer,” except in limited circumstances that are not relevant here.¹⁴⁸ Similarly, the Medicaid statute provides that “information disclosed by manufacturers . . . under [the MDRP] . . . is confidential and shall not be disclosed by [CMS] . . . in a form which discloses the identity of a specific manufacturer . . . [or] prices charged for drugs by such manufacturer,” except under limited circumstances that are not relevant here. Furthermore, the 340B Program generally protects the disclosure of information submitted by manufacturers participating in the program.¹⁴⁹ CMS should implement safeguards that ensure that information submitted under the Program is protected from disclosure to the same extent that such information is so protected under these federal laws and policies.

ii. Confidentiality Safeguards with Respect to the Public Explanation of the MFP

Lilly strongly urges CMS to adopt additional safeguards around the agency’s public explanation of the MFP. The statute requires CMS to publish such explanation of the MFP for each selected drug.¹⁵⁰ This public explanation poses an inherent risk of exposure of confidential commercial information given

¹⁴⁴ *Id.* § 1193(c).

¹⁴⁵ Guidance at 29.

¹⁴⁶ Guidance at 29; *see also* 45 C.F.R. §§ 5.41, 5.42.

¹⁴⁷ *See* 45 C.F.R. §§ 5.41, 5.42.

¹⁴⁸ SSA § 1847A(f)(2)(D) (subject to certain limited exceptions).

¹⁴⁹ *Id.* § 1927(b)(3)(D) (subject to certain limited exceptions).

¹⁵⁰ SSA § 1195(a)(2).

that the MFP likely will be based at least in part on drug pricing and other confidential commercial information. We recognize and appreciate CMS's stated intention to protect data elements containing non-public commercial or financial information from disclosure and to make only high-level comments about such information in the agency's public explanation of the MFP.¹⁵¹

However, Lilly believes that additional safeguards are needed to protect against **inadvertent** disclosure of proprietary information. Lilly recommends that CMS give manufacturers a reasonable opportunity to review the draft explanation in advance of public disclosure, including an opportunity to identify to CMS any way in which the draft explanation would directly or indirectly disclose manufacturers' confidential information. Doing so is well warranted given that Congress emphasized the need for confidentiality in the specific context of the public explanation of the MFP by explicitly cross-referencing the statute's confidentiality requirements in the provision requiring such explanation.¹⁵²

iii. Robust Storage and Access Controls

Lilly asks CMS to confirm that all trade secret, proprietary, and otherwise confidential commercial information of manufacturers will be stored in a secure manner with appropriate data privacy and security protections, as is necessary to protect sensitive information from inadvertent or malicious improper disclosure. Among other things, CMS should ensure that all confidential commercial information is stored appropriately in the Health Plan Management System (HPMS). We also ask that CMS specify how it intends to maintain similar confidentiality protections for information submitted to CMS via e-mail or Box. Among other things, we are concerned about the use of a third-party commercial platform like Box to collect voluminous amounts of proprietary information, and urge CMS to set forth the means by which the agency will ensure submitted information is kept confidential, including as against intentional or inadvertent misuse by Box personnel.

In evaluating other safeguards to better protect confidential records held by the agency, Lilly notes that CMS already implements many protections with respect to product and pricing data submitted by manufacturers participating in the MDRP. Under the MDRP, data are uploaded to an online interface that both state and manufacturer users access. Functionality of the interface, however, is limited by the user's role: State users do not have the ability to view quarterly or monthly pricing records or any product information because "some of this information is confidential (e.g., Baseline Average Manufacturer Price (AMP) data)."¹⁵³ To the extent not already accounted for, CMS should implement similar safeguards with respect to HPMS, and limit access by CMS staff to confidential information in HPMS only to situations where there is a programmatic need. CMS should also consider whether CMS's MDRP online interface includes other privacy and security protections that can be incorporated into the systems used to store confidential information under the Program to make such systems more robust in protecting the confidential information of manufacturers.

2. CMS's Must Abandon Its Proposed Policies Regarding Data Use and Destruction

- i. The Records Destruction Requirement Is Unenforceable Under the Terms of the Program Agreement, and, If CMS Were to Seek to Enforce It, Such Enforcement Would Be Violative of Manufacturers' Due Process Rights

¹⁵¹ Guidance at 29.

¹⁵² SSA § 1195(a)(2).

¹⁵³ CMS, *Medicaid Drug Programs (MDP) User Manual* 1 (Nov. 3, 2021).

As an initial matter, CMS's proposed requirement that a manufacturer destroy specified records, after the Program agreement terminates, is unenforceable. It is well-established that, when an agreement terminates, the obligations it imposes on parties terminate as well.¹⁵⁴ Thus, if a manufacturer declines to destroy such records after termination of the Program agreement, it violates no requirement of any such agreement. Accordingly, no CMP may be imposed.¹⁵⁵ CMS's observation that its own obligation to maintain the confidentiality of specified information "survive[s] termination of the Agreement"¹⁵⁶ does not alter the analysis. This is true because, as CMS acknowledges,¹⁵⁷ such information is protected from disclosure under FOIA, independent of whether a Program agreement is in force. Thus, as a requirement of the Program agreement established under section 1193(a)(5) of the SSA, the record destruction obligation ends with termination of the agreement, and therefore cannot be enforced after the agreement ceases to be in effect.

CMS must accede to this limitation against enforcement. If CMS were to treat the record destruction proposal as an enforceable requirement, it would raise serious questions of due process. As CMS knows, the statute imposes vast CMPs, including a CMP equal to \$100 million per piece of false information submitted by a small biotech drug or biosimilar manufacturer under section 1192(d)(2) or 1192(f)(1)(B) and \$1 million per day for a failure to submit required information.¹⁵⁸ The magnitude of these sanctions means that record-keeping is of paramount importance: Manufacturers must maintain complete records for evidentiary reasons to protect against mistaken penalties that could otherwise cost them hundreds of millions of dollars. By proposing to require that manufacturers destroy such records, the Guidance raises fundamental concerns under the Due Process Clause of the Fifth Amendment that would become ripe if the data destruction policy were treated as enforceable. "[T]he essence of due process is fundamental fairness," and little could be more fundamentally unfair than mandating destruction of the very records needed to verify an entity's innocence against erroneous penalty.¹⁵⁹ As the Supreme Court has long held, due process mandates a meaningful "opportunity to be heard."¹⁶⁰ Just as this includes the "opportunity to present reasons . . . why proposed action should not be taken," it must also include the right to maintain the evidence necessary to support such reasons.¹⁶¹

Enforcement of the record destruction proposal would also be patently arbitrary and capricious. Agency action is arbitrary and capricious if it "frustrate[s] the policy that Congress sought to implement."¹⁶² This describes exactly CMS's proposal. Mandated record destruction is irreconcilable with Congress's clear intent to establish a meaningful appeal process to challenge the imposition of a CMP. Specifically, section 1197(d) requires the Program to incorporate procedural requirements imposed under section 1128A. In turn, section 1128A(e) expressly provides that a party may "apply

¹⁵⁴ It is a "traditional principle that contractual obligations will cease, in the ordinary course, upon termination of the . . . agreement." *M&G Polymers USA, LLC v. Tackett*, 574 U.S. 427, 441–42 (2015) (citing *Litton Fin. Printing Div., Litton Bus. Sys., Inc. v. NLRB*, 501 U.S. 190, 207 (1991)).

¹⁵⁵ See SSA § 1198(c) (authorizing the imposition of a CMP of \$1 million per day only for a violation of a requirement of a Program agreement established under section 1193(a)(5)); see also *id.* § 1193(a)(5).

¹⁵⁶ Guidance at 29.

¹⁵⁷ *Id.* at 28–29.

¹⁵⁸ *Id.* at 69–70.

¹⁵⁹ *Evans v. Wilkerson*, 605 F.2d 369, 371 (7th Cir. 1979).

¹⁶⁰ *Mathews v. Eldridge*, 424 U.S. 319, 333 (1976) (internal quotation marks omitted).

¹⁶¹ See *Cleveland Bd. of Educ. v. Loudermill*, 470 U.S. 532, 546 (1985) (citing Friendly, "Some Kind of Hearing," 123 U. Pa. L. Rev. 1267, 1281 (1975)).

¹⁶² *Mylan Labs. Ltd. v. FDA*, 910 F. Supp. 2d 299, 306 (D.D.C. 2012).

to the court for leave to adduce additional evidence and shall show to the satisfaction of the court that such additional evidence is material.”¹⁶³ CMS may not impose a record destruction requirement that subverts the clear intent of this provision, which is to enable a party to present any material evidence to a court when a case is heard on appeal, without violating the prohibition against arbitrary and capricious agency action.¹⁶⁴

ii. The Manufacturer Gag Rule Violates Manufacturers’ Free Expression Rights and Threatens Unconstitutionally Excessive Fines

CMS’s proposed gag on manufacturer disclosure of negotiation-related information violates manufacturers’ basic First Amendment “right to speak freely.”¹⁶⁵ The proposal would compel manufacturer silence as to information highly relevant to political discourse—i.e., the government’s administration of a major program that implicates a far-ranging set of fundamental equities—through the threat of a CMP of \$1 million per day for as long as the Program agreement is in effect.¹⁶⁶ Should a manufacturer make any of a broad swath of program-related information publicly available, as is its right under the Free Speech Clause of the First Amendment, it could be penalized with boundless CMPs for as long as the Program agreement is in effect, as there would be no ability to “un-ring the bell” and thereby come back into compliance and cut off the CMPs. Such an unprecedented burden on free speech cannot be countenanced. As the Supreme Court has admonished, government “may no more silence unwanted speech by burdening its utterance than by censoring its content.”¹⁶⁷

Not only does CMS’s proposal not withstand heightened scrutiny, but it is not even rationally defensible. In fact, the federal government imposes no comparable requirement with respect to drug price negotiations under the Federal Supply Schedule (FSS) program administered by the Department of Veterans Affairs (VA). FSS agreements contain no language prohibiting a manufacturer from disclosing negotiation-related information. Especially in light of how the federal government administers the FSS program, there is no justification for the proposed severe speech restriction under the Program.

The prospect of effectively boundless CMPs also raises grave concerns under the Eighth Amendment’s prohibition against excessive fines. “The touchstone of the constitutional inquiry under the Excessive Fines Clause is the principle of proportionality.”¹⁶⁸ It is difficult to envision anything more “grossly disproportional” than the prospect of a million dollar penalty per day that could perpetuate for years or even decades – even more so because the penalty is imposed where there is no “loss to the public fisc,” and the manufacturer is simply exercising its constitutional right to speak freely.¹⁶⁹

3. The Gag Rule Is Irreconcilable with Corporate Fiduciary Duties and May Result in

¹⁶³ SSA § 1128A(e).

¹⁶⁴ See 5 U.S.C. § 706(2)(A).

¹⁶⁵ *Wooley v. Maynard*, 430 U.S. 705, 714 (1977).

¹⁶⁶ See Guidance at 69. Consistent with the discussion above, CMS’s proposed gag on manufacturers is unenforceable once the Program agreement terminates. The silence it imposes on manufacturers exists as a requirement of the Program agreement, which terminates with the agreement, as does the agency’s ability to impose a CMP for a violation of the agreement.

¹⁶⁷ *Sorrel v. IMS Health Inc.*, 564 U.S. 552, 566 (holding that a law compelling silence by pharmaceutical manufacturers with respect to certain pharmacy records violated the First Amendment).

¹⁶⁸ *United States v.ajakajian*, 524 U.S. 321, 334 (1998).

¹⁶⁹ *Id.* at 323-24.

Liability Under Federal and State Securities Laws

Manufacturers also cannot be subject to “gag” requirements that bar them from sharing material information with key constituents, including their boards and shareholders. Among other things, manufacturers have obligations to make material information available to shareholders and must maintain records to facilitate this obligation.¹⁷⁰

The proposed data use and destruction provisions will restrict important information from making its way into markets, resulting in potential liability for manufacturers under applicable federal and state securities laws. For example, were a public company to discuss its expectations regarding market share for a drug under development, and then later learn through the MFP setting process that it is unlikely to achieve the market share previously expected, it would be appropriate to use that information to update the market and reset expectations. Under CMS’s proposal, the company could not do so.

This could raise fundamental questions as to whether a company has violated its legal duties to update statements previously made to shareholders and potential shareholders – potentially exposing the company to vast liability for failing to provide material information to investors. Similar concerns can arise with private companies, which are subject to anti-fraud provisions of applicable federal and state securities laws. If a private company does not disclose information that is later viewed as material, it risks liability for failure to disclose that information. Hiding information from investors, whether public or private, runs contrary to the fundamental underpinnings of U.S. securities laws, which expect sunlight and visibility into important developments related to companies.

The Guidance’s generic exception to the gag requirement (“except as may required by applicable . . . law”) also does not address these concerns. In many cases there will not be bright line requirements under applicable law, leaving companies uncertain as to what they may and may not do to comply with their competing obligations.¹⁷¹

VII. Setting the MFP: Special Considerations

- A. CMS Should Allow Manufacturers to Submit Evidence Demonstrating That Pricing Below a Specified Level Would Imperil Patient Access, and CMS Should Specify That the MFP Will Not Be Set Below That Price (or the MFP Ceiling Price If Lower)*

Government price-setting has been shown by research to have profoundly negative impacts on innovation and thus impede patient access to critical therapies. For example, one study in Europe found that a “10% drop in the price of medicines in price-controlled [European Union] markets was associated with . . . an 8% increase in the delay of access to medicines.”¹⁷² Other studies have shown that reductions in pharmaceutical revenues caused by pricing regulation reduce the annual number

¹⁷⁰ Under nearly all states’ corporate laws, corporations are required to maintain records and permit shareholders to inspect their books and records. *See, e.g.*, 8 Del. C. § 220 (describing the power of a shareholder to demand inspection of a corporation’s books and records).

¹⁷¹ Guidance at 30.

¹⁷² D. Schulthess and H. Bowen, *The Historical Impact of Price Controls on the Biopharma Industry*, Vital Transformations (Nov. 22, 2021).

of marketed therapies.¹⁷³ Research has also demonstrated that government price-setting is associated with drastic declines in early stage research, which is the precursor to robust future transformational therapeutic innovation.¹⁷⁴ The adverse consequences of discouraging innovation are ultimately borne by patients, who are prevented from accessing the most effective treatments.¹⁷⁵

There may be instances where a manufacturer demonstrates that setting the MFP below a particular price would imperil patient access to the selected drug. In other words, such a mandated price would be so far below the market price that a mismatch between supply and demand would result. To protect patient access to medicines, we urge CMS to specify that, in such cases, it will not set the MFP below the lower of such price or the MFP ceiling price. Patient access should be a paramount consideration in interactions with manufacturers to set the MFP, and CMS should develop policies to specifically account for this concern to mitigate the negative impact on patients that could follow from the imposition of an unreasonably low MFP.

B. CMS Should Clarify That It Will Not Set the MFP Below the MFP Ceiling Price During Any Year of the Price Applicability Period During Which the Drug Is Under Patent Protection

As part of the MFP setting process, the statute requires CMS to consider a number of factors in setting the MFP for a selected drug, including “[d]ata on pending and approved patent applications [and] exclusivities recognized by [FDA].”¹⁷⁶ In the Guidance, CMS indicates that, if a selected drug has patents and exclusivities that will last a number of years, CMS may adjust the “preliminary price” downward.¹⁷⁷ Lilly strongly urges CMS to change course, and instead afford pricing relief based on whether, based on information submitted by the manufacturer, a selected drug will have any remaining patent protection at the start of the price applicability period that cannot be designed around (the basic drug substance patent) or that cannot be avoided via a “skinny label” (collectively, the “primary patents”). If it will, CMS should set the MFP at the MFP ceiling price during any year of the price applicability period during which the drug is under such patent protection.

The statute permits CMS to subject a drug to MFP setting at least seven years post-approval and a biologic at least eleven years post-approval.¹⁷⁸ In many cases, by the time the price applicability period for a selected drug begins, the product’s regulatory exclusivity period will have expired—but this is not necessarily the case for its patent protection period.¹⁷⁹ Patents afford longer exclusivity periods, meaning that it may very well be the case that there will be remaining patent protection for a selected drug that extends into the price applicability period.

It is vital that selected drugs still under patent protection be given special protection. The process of bringing pharmaceutical or biotechnology product from research and development to market is

¹⁷³ See, e.g., D. Acemoglu & J. Linn, Market Size in Innovation: Theory and Evidence from the Pharmaceutical Industry, Q. J. of Econ., Vol. 119 (2004).

¹⁷⁴ See T. Abbott & J. Vernon, The Cost of US Pharmaceutical Price Reductions: A Financial Simulation Model of R&D Decisions, 28 Managerial & Decision Econ. 293 (2007).

¹⁷⁵ See N. Sood, et al., *The Effect of Regulation on Pharmaceutical Revenues: Experience in Nineteen Countries*, 28 Health Affairs 11 (2009).

¹⁷⁶ SSA § 1194(e)(1)(D).

¹⁷⁷ Guidance at 53.

¹⁷⁸ SSA § 1192(e)(1)(A)-(B).

¹⁷⁹ See FDA, Frequently Asked Questions on Patents and Exclusivity, available at <https://www.fda.gov/drugs/development-approval-process-drugs/frequently-asked-questions-patents-and-exclusivity#howlongexclusivity> (last accessed Feb. 2023).

exorbitantly long and expensive.¹⁸⁰ Many candidates fail despite significant investment. In a 2021 study of research and development costs, the Congressional Budget Office (CBO) found that “[t]he amount of money that drug companies devote to [research and development] is determined by the amount of revenue they expect to earn from a new drug, the expected cost of developing that drug, and policies that influence the supply of and demand for drugs.”¹⁸¹ The CBO also found that estimates of the average research and development costs for new drugs range from less than \$1 billion to more than \$2 billion, while only about 12% of all drugs that enter clinical trials are ultimately approved by FDA.¹⁸²

The patent system, like regulatory exclusivities, is designed to recognize the risks and costs inherent in innovation and reward such investment in research and development. Indeed, courts have expressly recognized that “the encouragement of investment-based risk is the fundamental purpose of the patent grant.”¹⁸³ It is the patent protection period that affords a manufacturer the opportunity to recover its research and development costs – not only for the drug for which the patent was awarded but also for other research and development investments that the manufacturer may have made. Simply put, the risk associated with bringing, and the investment required to bring, a new drug to market dwarfs the corresponding risk and investment for a copy product. From a technical perspective, the entry barrier for a new drug is sky high relative to that of the corresponding copy product.

CMS should take special care not to upset the long-standing policy designs of the U.S. patent system. It can do so by honoring any remaining patent period for selected drugs by specifying that the MFP will not be set below the MFP ceiling price for during any year during the price applicability period into which the drug’s patent protection period extends.

C. For a Small Molecule Drug, CMS Should Specify That It Will Not Set the MFP Below the MFP Ceiling Until at Least the First Year of the Price Applicability Period That Starts After the Date on Which Thirteen Years Have Lapsed Since Its Approval

To be MFP-eligible, biologics (large molecules) must be at least eleven years post-licensure, while drugs (small molecules) must be at least seven years post-approval.¹⁸⁴ The approximately two-year time lag between selection for the MFP process and application of the MFP means that an MFP cannot apply to a biologic until at least approximately **thirteen** years after licensure, whereas an MFP cannot apply to a drug until at least approximately nine years post-approval. CMS should set the MFP at the MFP ceiling until at least the first year during the price applicability period that starts at least **thirteen years after** the approval of a drug. This approach is necessary to help preserve small molecule innovation in parity with large molecule innovation.

¹⁸⁰ See also, e.g., Henry Grabowski, et al., Continuing trends in U.S. brand-name and generic drug competition, 24 J. Med. Econ. 908, 914 (2021) (finding that the average 2017-19 MEP of 13.0 years for new molecular entities (NMEs) of more than \$250 million has changed relatively little over the past decade and remains lower than for all NMEs (14.1 years). Paragraph IV challenges are more frequent and occur earlier for NMEs >\$250 million. Generic share erosion remains high for both NME types.

¹⁸¹ CBO, Research and Development in the Pharmaceutical Industry (Apr. 8, 2021), available at <https://www.cbo.gov/publication/57126>.

¹⁸² *Id.*

¹⁸³ *BIO v. District of Columbia*, 496 F.3d 1362, 1372 (Fed. Cir. 2007).

¹⁸⁴ SSA § 1192(e)(1).

In particular, Lilly is concerned that the nine- and thirteen-year distinction arbitrarily promotes large molecule biologic innovation to the detriment of small molecule drug innovation. Studies show that, in the first five years on the market, most products (whether small or large molecules) achieve modest levels of annual sales.¹⁸⁵ Accordingly, manufacturers may seek the economic benefit of an additional four-year shelter from selection for the MFP process by focusing research and development on biologics instead of drugs.

Disincentivizing manufacturers from investing in small molecule drugs presents serious risk to patient access to effective treatments. Studies have shown that biologics account for 37% of net drug spending in the United States and are estimated to cost 22 times more than small molecule drugs.¹⁸⁶ Such costs are prohibitive for many patients. Small molecule drugs, on the other hand, are generally less expensive to develop and produce than biologics. Lower production costs translate into lower drug prices, increasing accessibility for patients. Nevertheless, small molecule drugs do not enjoy the same additional four years of freedom from selection for the MFP process that biologics enjoy.

Moreover, while patients benefit from access to both types of products, small molecule drugs figure more prominently in the treatment plans of most Americans. Many biologics must be stored and administered in specialized clinics under the supervision of medical professionals.¹⁸⁷ One reason for this restriction is that biologics (which are produced from living organisms) require strict control over storage and handling that is often unnecessary for more stable chemically-derived small molecule drugs.¹⁸⁸ Also, with respect to a biologic, medical professional supervision may be necessary to administer care if the patient suffers from a serious, life-threatening side effect, such as an unintended immune response to the product. As a result, patient access to biologic treatments may be limited by geographic and/or time constraints. Small molecule drugs, by contrast, are more easily administrated and more readily mobile.

Accordingly, CMS should promote small molecule drug development to the greatest extent possible by setting the MFP for a small molecule drug at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval thereby helping to counterbalance the incentives that place a disproportionate emphasis on biologic development at the expense of small molecule drug development.

D. CMS Should Ensure Continued Manufacturer Participation in the Program – and Access for Patients to the MFP – by Including Meaningful Protections for Manufacturers Against “Spillover” Risks

Since the enactment of the IRA, several states have proposed legislation that would authorize or require the state to rely on a selected drug’s MFP as a reference point in setting a price or payment

¹⁸⁵ Quintiles IMS Inst., *Lifetime Trends in Biopharmaceutical Innovation: Recent Evidence and Implications*, at 2 (Jan. 2017).

¹⁸⁶ A. Roy, *Biologic Medicines: The Biggest Driver of Rising Drug Prices*, *Forbes*, Mar. 8, 2019, available <https://www.forbes.com/sites/theapothecary/2019/03/08/biologic-medicines-the-biggest-driver-of-rising-drug-prices/?sh=520ce94118b0>; F. D. Makurvet, *Biologics vs. Small Molecules: Drug Costs and Patient Access*, 9 *Medicine in Drug Discovery* 1,4 (2021).

¹⁸⁷ T. Morrow & L. H. Felcone, *Defining the difference: What Makes Biologics Unique*, 1 *Biotechnology Healthcare* 24 (2004).

¹⁸⁸ *Id.*

limit outside of the Medicare market.¹⁸⁹ And at least one state agency has promulgated regulations authorizing the state's Prescription Drug Affordability Board to consider a selected drug's MFP in setting an upper payment limit for the drug, as subject to an affordability review.¹⁹⁰ It is also possible that commercial entities will seek to invoke the MFP as a reference price in commercial negotiations. However, MFPs are not reference prices or objective external benchmarks; they are prices that manufacturers, based on forced disclosure of highly sensitive data, are compelled to make available with respect to Medicare beneficiaries because failure to do so will result in a penalty (styled as an excise tax) of up to 1900% of daily sales and/or effective exclusion from doing business with Medicare and Medicaid.

The MFP is not designed to serve as a reference price or external benchmark across non-Medicare markets. Indeed, broad spillover of this compelled price could engender risks to all federal healthcare program beneficiaries because widespread and unintended reliance on the MFP (by states or commercial entities) will make it impossible for manufacturers to continue to participate in federal programs at all. This is why Congress explicitly restricted the obligation to provide access to the MFP to units furnished or dispensed to **Medicare** beneficiaries.

The MFP is also not a rational metric for statewide drug pricing or payment restrictions—because it is not set by reference to any objective metric tied to the appropriate price or payment that should be applied to a drug across any given state market. Further, expanding the application of the MFP outside of the Medicare market risks fundamentally disrupting the careful balance that Congress struck in establishing the Program thereby jeopardizing patient access and impeding innovation.¹⁹¹ It would, for example, greatly skew the projected revenue and sales volume for a selected drug as well as the return on investment in research and development costs, factors that CMS must consider in setting an MFP.

More fundamentally, if the MFP is used as a reference point for non-Medicare markets, manufacturers will be unable to invest in ongoing innovation because they will face undue limitations on their ability to recoup the potentially billions of dollars in research and development costs associated with developing a single drug, much less the countless additional billions of dollars spent on research and development that never culminate in an approved product.¹⁹² Congress did not intend for the Program to grind the wheels of innovation to a halt, and unambiguously limited the scope of the MFP accordingly.

It is imperative that CMS address need to protect incentives for innovation by limiting the expansion of the MFP beyond the Medicare market and, thus, outside of the scope intended by Congress. To mitigate these serious concerns, Lilly asks CMS to address this in the Program agreement. We think there are at least two options. First, CMS could specify in the agreement that the MFP will not be set below the MFP ceiling price where the manufacturer shows that the MFP will be or has been used as

¹⁸⁹ See, e.g., S.B. 967, Va. Gen. Assembly (2023) (providing that the prescription drug affordability board “may adopt the Medicare maximum fair price . . . for a prescription drug product as the upper payment limit amount”); H.F. 17, Minn. Leg., 93rd Sess. (2023) (“When setting an upper payment limit for a drug subject to the Medicare maximum fair price under United States Code, title 42, section 1191(c), the board shall set the upper payment limit at the Medicare maximum fair price.”).

¹⁹⁰ 3 Colo. Code Regs. § 702-9:4.1(C)(2)(a)(ix).

¹⁹¹ See D. Schulthess and H. Bowen, *The Historical Impact of Price Controls on the Biopharma Industry*, Vital Transformations (Nov. 22, 2021).

¹⁹² See M. Schlander, et al., *How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment*, *PharmacoEconomics* 1243–1269 (2021).

a reference point in setting a pricing or payment limit outside of the Medicare market. Alternatively, CMS could specify that, where there is a non-trivial amount of spillover of MFP pricing outside the Medicare market (say 5% of unit sales), that constitutes a “material change” to the agreement that triggers a “renegotiation.”

E. CMS Should Specify That the MFP Will Not Be Set Below Ceiling Price if the Selected Drug Is Subject to a VBP Subject to the MBPRO

CMS has repeatedly expressed a strong interest in promoting value-based pricing of and payment for drugs and biologics to promote access to the highest quality of care available while also achieving cost savings within its programs and across the health care system more generally.¹⁹³

In 2020, CMS promulgated a rule to better promote VBPs in the commercial and Medicaid marketplaces in light of historical obstacles under the MDRP by establishing the MBPRO.¹⁹⁴ The MBPRO is a new option for reporting BP where a manufacturer offers a VBP in the commercial market. Manufacturers that elect to report via the MBPRO are required to submit two distinct sets of BP data: (1) the set of potential BPs available under the VBP (VBP BP), which reflect the multiple value-based prices available under the arrangement; and (2) a single non-value-based BP (non-VBP BP), which reflects the lowest price available from the manufacturer outside of the VBP.¹⁹⁵ MBPRO ensures that state Medicaid programs have a choice between (1) participating in the VBP, in which case the Medicaid rebate amount is calculated based on the VBP BP, and (2) not participating in the VBP, in which case the Medicaid rebate amount is calculated based on the non-VBP BP.

In establishing the MBPRO, CMS recognized the “interest among patient and consumer groups, states, and manufacturers in the new multiple best price policy” in light of the shift to value-based pricing and payment that it represents.¹⁹⁶ CMS also stated that the policy “is meant to help improve patient access to new medications, particularly new high cost therapies such as gene or cell therapies, by facilitating the use of VBP arrangements when purchasing such medications.”¹⁹⁷

More recently, the Center for Medicare and Medicaid Innovation (CMMI) proposed a set of innovative models to further value-based pricing and payment, including a Cell and Gene Therapy Access Model that will enable CMS to coordinate and administer outcomes-based agreements with manufacturers of certain cell and gene therapies on behalf of state Medicaid programs.¹⁹⁸ This VBP-oriented model is consistent with the stated policy priorities of the Biden Administration. In fact, the model was in direct response to an Executive Order issued by President Biden on October 14, 2022, requiring HHS to consider models that “would lower drug costs and promote access to innovative drug therapies for beneficiaries enrolled in the Medicare and Medicaid programs,” including through the use of

¹⁹³ See, e.g., 85 Fed. Reg. 87,000, 87,032 (Dec. 31, 2020); 83 Fed. Reg. 22,692 (May 16, 2018) (explaining that “[v]alue-based transformation of our entire healthcare system is a top [Department of Health and Human Services (HHS)] priority”); CMS, What are the value-based programs? (last accessed Feb. 2023), available <https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/Value-Based-Programs/Value-Based-Programs>.

¹⁹⁴ 85 Fed. Reg. at 87,032.

¹⁹⁵ 85 Fed. Reg. at 87,025.

¹⁹⁶ 86 Fed. Reg. 28,742, 28,744 (May 28, 2021).

¹⁹⁷ 85 Fed. Reg. at 87,032.

¹⁹⁸ HHS, HHS Secretary Responds to the President’s Executive Order on Drug Prices (Feb. 14, 2023), available at <https://www.hhs.gov/about/news/2023/02/14/hhs-secretary-responds-to-the-presidents-executive-order-on-drug-prices.html>.

“value-based payment that promotes high quality care.”¹⁹⁹

CMS should take special care to ensure that the Program does not undermine the very VBPs that CMS is seeking to advance through the host of initiatives described above. One way to do so is to specify that, where a manufacturer submits information during the MFP setting process showing that it offers a VBP for a selected drug and has elected the MBPRO or is participating in a VBP-oriented model, CMS will not set the MFP for the drug below the MFP ceiling price. Doing so will further the agency’s policy objective of promoting value-based pricing of and payment for drugs by incentivizing VBPs.

VIII. MFP Ceiling: Average Non-FAMP

Lilly respectfully recommends that CMS address the following points related to the average Non-FAMP and the calculation of MFP ceiling price.

A. The basis of the “average Non-FAMP”

The statute requires CMS to use an “average Non-Federal Average Manufacturer Price” (average Non-FAMP) as part of determining the ceiling for the MFP. In the Guidance, CMS signals its intent to develop, implement, and oversee a completely new pricing program to calculate the average Non-FAMP based on information collected over each given **calendar** year.²⁰⁰ Lilly strongly opposes this proposal as unnecessary, burdensome, and inconsistent with Congress’s intent. CMS should instead adopt an approach for calculating the average non-FAMP that simply adopts the annual Non-FAMP under the Veterans Health Care Act of 1992 (VHCA), which is based on the federal **fiscal** year.

In the first place, borrowing from the existing VHCA framework would generate vast efficiencies for both the agency and manufacturers. If CMS were to use the existing VHCA framework, there would be no need for CMS to create and oversee a completely new price reporting framework, which would save countless resources for both the agency and manufacturers.

Calculating the average Non-FAMP in a manner that aligns with the VHCA framework would also better align with Congress’s intent. The average Non-FAMP is statutorily defined to “mean[] the average of the non-Federal average manufacturer price (as defined in section 8126(h)(5) of title 38, United States Code) for the 4 calendar quarters of the year involved.”²⁰¹

The statutory cross-reference to 38 U.S.C § 8126(h)(5) is to the **VHCA**. As such, the statute effectively directs CMS to start with the Non-FAMP calculations under the VHCA to determine how to calculate the average Non-FAMP.

Under the VHCA, manufacturers are required to calculate and report quarterly Non-FAMPs and an annual Non-FAMP, and the annual Non-FAMP is calculated based on quarterly data from the federal **fiscal** year (not the calendar year).²⁰² Given the explicit statutory reference to the VHCA in the

¹⁹⁹ Executive Order No. 14087, 87 Fed. Reg. 63,399, 63,399–400 (Oct. 14, 2022).

²⁰⁰ Guidance at 42-44.

²⁰¹ SSA § 1194(c)(6).

²⁰² For example, for the 2021 annual Non-FAMP (a benchmark average Non-FAMP year referenced in the statute), the data used for the calculation covers the period of October 1, 2020, through September 30, 2021 (Q4 (CY1) through Q3 (CY2)). See SSA § 1194(c)(1)(C). Note that quarterly non-FAMP calculations themselves

average Non-FAMP definition, there is every reason to think that Congress wanted the Program's calculation of the average Non-FAMP to align with the VA's long-standing approach to calculating the annual Non-FAMP. As such, use of a federal **fiscal** year is the most appropriate way to calculate the average Non-FAMP. Lilly acknowledges that the statute specifies that the average Non-FAMP is calculated based on the "4 calendar quarters of the year involved," but the statute leaves room for use of a federal fiscal year-based approach because it does not specify whether the "year involved" is a calendar year or a federal fiscal year. This gives CMS ample discretion to base the average Non-FAMP calculation on the four quarters of the federal fiscal year (Q4 – Q3) to promote alignment between the average Non-FAMP calculation and the pre-existing VHCA calculation of the annual Non-FAMP.

It is also critical that CMS develop mechanisms to account for anomalies in the average Non-FAMP and to permit restatements of the average Non-FAMP due to data or other errors identified after the fact. The VA's experience under the VHCA has shown that issues inevitably arise that yield anomalous or erroneous non-FAMP-related calculations. Just as the VA has done, CMS must develop exceptions processes to account for such issues, irrespective of whether it calculates the average Non-FAMP using a calendar year- or a federal fiscal year-based approach.

Below, Lilly notes the following comments and considerations bearing on exceptions processes:

- *Average Non-FAMP Anomalies:* Anomalous Non-FAMPs can occur when sales dollars and units misalign. This can result from lagged sales, market shortages, or other factors. VA has recognized this and, in implementing the VHCA program, has developed certain exceptions and workarounds for calculating federal ceiling prices (FCPs) when there are anomalous Non-FAMPs. Similarly, CMS must develop an approach to addressing anomalous average Non-FAMPs for purposes of setting the MFP. In certain cases, use of a prior year's figures may be best, but there may be cases involving new products or other scenarios where use of the prior year's figures is not possible.
- *Restated Average Non-FAMPs:* VA also has recognized the need for a process to allow manufacturers to restate Non-FAMPs in cases where reported Non-FAMPs are determined to have been inaccurate, as a result of flaws in sales data, issues impacting data systems, and other factors. As such, restatements are not uncommon, and contract pricing can be adjusted based on restated Non-FAMP and FCPs. While VA handles restatements of annual Non-FAMPs, if CMS proceeds with its proposed calendar year-based average Non-FAMP computations, it must address any calculation errors that could arise. Additionally, in any case involving average Non-FAMP restatement, CMS must establish a process for account for such restatement in the setting of the MFP.

B. The 12/16 Year Time Period Used to Identify an "Extended" or "Long" Monopoly Drug Is Measured from the Date of the Approval/Licensure to the Start of the Applicable IPAY, Not the Date of the Selection.

The statute sets the ceiling price for the MFP for selected drugs by reference to three disjunctive options. Two of the options are notably based on the "applicable percent" of the applicable average Non-FAMP:

are not used to calculate the annual Non-FAMP. Rather, the annual Non-FAMP is a stand-alone weighted average calculation based on data over 4 quarters: Q4 – Q3.

- (1) An amount equal to the **applicable percent** of the average non-FAMP for 2021 (or, where there is none, the average non-FAMP for the first full year following market entry), increased by the percentage increase in the Consumer Price Index for All Urban Consumers from September 2021 to September of the year prior to the selected drug publication date (or, December of the first full year following the market entry); and
- (2) An amount equal to the **applicable percent** of the average non-FAMP for the year prior to the selected drug publication date (except for IPAY 2026).²⁰³

The “applicable percent” is, in turn, statutorily defined by reference to whether a drug is classified as a short-monopoly drug (75%), extended-monopoly drug (65%), or long-monopoly drug (40%).²⁰⁴ Pursuant to the statute, these classifications are primarily based on the number of years that have elapsed since a product was approved or licensed. With limited exceptions, an extended-monopoly drug is, “with respect to an initial price applicability year, a selected drug for which at least 12 years, but fewer than 16 years, have elapsed since the date of approval . . . or . . . licensure,” and a long-monopoly drug is, “with respect to an initial price applicability year, a selected drug for which at least 16 years have elapsed since the date of approval . . . or licensure.”²⁰⁵ Any other selected drug is a short monopoly drug.²⁰⁶

With respect to extended- and long-monopoly drugs, the most natural reading of the statutory text is that the twelve- and sixteen-year periods run from the selected drug’s approval or licensure date **to the start of its IPAY**. This comports with a plain reading of the statute, which expressly references the “initial price applicability year” and juxtaposes such reference with the date of approval or licensure.

Moreover, doing otherwise would lead to anomalous situations where a drug transitions from one classification to another **after** the MFP is set but **before** the MFP applies, e.g., where a drug is selected for the MFP process fifteen years after its approval but is seventeen years post-approval by the start of its IPAY. This cannot be what Congress intended – because the MFP would be negotiated based on an MFP ceiling calculated for an extended-monopoly drug but the drug would be a long-monopoly drug when the MFP starts to apply.

The Guidance is internally inconsistent. In one passage, CMS appears to propose to count the years to the date of selection.²⁰⁷ In another, the agency appears to propose to count the years to the start of the applicable IPAY.²⁰⁸ To ensure a workable system, Lilly recommends that CMS adopt a policy under which the years are counted from the date of approval or licensure to the start of the applicable IPAY. This approach comports with the natural reading of the statute and will eliminate irregularities.

IX. Application of the MFP

- A. *CMS Should Revise Its Proposed Methodology for Applying the MFP Across the Dosage Forms and Strengths of a Selected Drug Such That the Dosage Form/Strength-Level MFP Is Capped by the MFP Ceiling Only at the Drug Level and Not Also at the Dosage Form/Strength-Level.*

²⁰³ SSA § 1194(c)(1)–(2).

²⁰⁴ *Id.* § 1194(c)(3).

²⁰⁵ *Id.* § 1194(c)(4)(A), (c)(5)(A).

²⁰⁶ *Id.* § 1194(c)(3)(A).

²⁰⁷ Guidance at 45.

²⁰⁸ *Id.* at 17.

By statute, CMS must “establish[] procedures to compute and apply the [MFP] across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug.”²⁰⁹ Given the complexities inherent in applying a single MFP across varying dosage forms and strengths, it is essential that the calculation be predicated on a transparent methodology, and one that finds support in the statute.

In the Guidance, CMS proposes to “translate the MFP once finalized . . . back into per unit (e.g., tablet) prices at the dosage form and strength level for the purposes of publishing per unit MFPs for the different dosage forms and strengths of the selected drug.”²¹⁰ Specifically, for IPAY 2026, CMS proposes to translate the MFP at the **drug** level into a price for each **dosage form or strength** at the **unit** level, as follows:²¹¹

1. **Cap the drug-level MFP by comparing such MFP to the lower of the two alternative drug-level ceiling prices:** Compare the MFP per thirty-day equivalent supply at the **drug** level to the lower of the two alternative ceiling prices, which are also calculated per thirty-day equivalent supply at the drug level. If the MFP is higher than the lower of the two ceiling prices, reduce the MFP so that it is equal to the lower of the two ceiling prices.²¹² The result is an MFP per thirty-day equivalent supply at the **drug** level.
2. **Weighted average wholesale acquisition cost (WAC) for each dosage form and strength:** Calculate a weighted average WAC at the **dosage form or strength** level per thirty-day equivalent supply, based on 2022 Part D PDE data.²¹³
3. **Weighted average WAC for the drug:** Use the weighted average WAC for each dosage form and strength, calculated at Step 2, to calculate a weighted average WAC per thirty-day equivalent supply at the **drug** level.²¹⁴
4. **WAC ratio for each dosage form and strength:** Calculate a WAC ratio for each dosage form and strength by dividing the weighted average WAC for each dosage form and strength, calculated in Step 2, by the weighted average WAC for the drug, calculated in Step 3.²¹⁵
5. **Dosage form/strength-level MFP:** Translate the single **drug**-level MFP, as capped in Step 1, into a **dosage form/strength**-level MFP by multiplying the single drug-level MFP by the WAC ratio calculated in Step 4 for each dosage form and strength. The result is an MFP per thirty-day equivalent supply at the **dosage form or strength** level.²¹⁶
6. **Cap (a second time) the dosage form/strength-level MFP by comparing such MFP to the dosage form/strength-level ceiling price:** Compare the dosage form/strength-level MFP, as calculated in Step 5, to the applicable dosage form/strength-level ceiling price (separately calculated as part of determining the ceiling price at the drug level used in Step 1). If the dosage form/strength-level MFP is higher than the applicable dosage form/strength-level

²⁰⁹ SSA § 1196(a)(2).

²¹⁰ Guidance at 38, 58-59.

²¹¹ A more complete summary of our understanding of this process is set forth in Appendix A.

²¹² Guidance at 48.

²¹³ *Id.* at 58 (CMS’s Steps 1 through 4).

²¹⁴ *Id.* at 59 (CMS’s Steps 5 through 7).

²¹⁵ *Id.* (CMS’s Step 8).

²¹⁶ *Id.* at 59 (CMS’s Step 9).

ceiling price, reduce the dosage form/strength-level MFP so that it is equal to the applicable dosage form/strength-level ceiling price.²¹⁷

7. **Per-unit dosage form/strength-level MFP:** For each NDC-9 of a dosage form and strength, calculate the MFP per thirty-day equivalent supply on the unit level by dividing the result from Step 6 by the units per total thirty-day equivalent supply for the dosage form and strength.²¹⁸

As set forth above, CMS proposes to apply the MFP ceiling **twice** – a first time at the **drug** level (Step 1) and a second time at the **dosage form or strength** level (Step 6). **CMS should not – and indeed may not – finalize this proposal.**

Double application of the ceiling price – at the drug level and, again, at the dosage form and strength level – finds no basis in law. The statute defines both the MFP and the ceiling price as a price determined at the **drug** level.²¹⁹ Nowhere does the statute contemplate the application of the ceiling price at the **dosage form or strength** level. To be sure, the statute directs CMS to establish a process to **apply** the MFP (which **already** has been capped by the ceiling price) to each dosage form and strength of the selected drug, but, in doing so, the statute does not authorize the application of the ceiling price a second time. The proposed double application of the ceiling price would violate the statute's clearly defined processes governing how to **cap** the MFP of a selected drug and, **separately**, how to **apply** such MFP across the dosage forms and strengths of such drug.

As a matter of fact, the application of the ceiling price a second time, at the dosage form and strength level, could cause the MFP of some dosage forms and strengths of a selected drug to be reduced a second time as demonstrated by the numeric example in Appendix A. A WAC ratio for a dosage form or strength **higher than 1.0** could generate a dosage form/strength-level MFP that is **above the dosage form/strength-level ceiling price**, and thus a dosage form/strength-level MFP that is doubly capped. Double capping the dosage form/strength-level MFP would unfairly penalize dosage forms and strengths with a higher WAC ratio, even though such higher WAC ratio could merely reflect a difference in utilization, such as a difference in dosing regimen or a higher Part D utilization.

In addition to abandoning its unlawful proposal to doubly apply the ceiling price, CMS should clarify the following:

- **First, CMS should specify how it will calculate the thirty-day equivalent supply and the total thirty-day equivalent supply.** Specifically, Lilly asks that CMS clarify that the definition of a thirty-day equivalent supply is the same as that used under the Part D program to calculate the cost thresholds for specialty tiers under which CMS determines the 30-day equivalent supply as follows: If the days' supply reported on a PDE is less than or equal to 34, the number of 30-day equivalent supplies equals one. If the days' supply reported on a PDE

²¹⁷ Specifically, CMS states that it “intends to ensure that the MFP per 30-day equivalent supply for each dosage form and strength of the selected drug calculated in step 9 of the methodology described in section 60.5 of this memorandum is not above the statutorily defined ceiling by comparing it to the applicable ceiling for a 30-day equivalent supply for that dosage form and strength of the selected drug calculated in either step 7 of section 60.2.2 or step 9 of section 60.2.3 (depending on which ceiling is selected).” *Id.* at 46.

²¹⁸ *Id.* at 59 (CMS's Step 10).

²¹⁹ See, e.g., SSA § 1194(c) (describing the ceiling price by reference to a drug). The reference to a drug, as opposed to a dosage form or strength, is telling, given that, elsewhere in the statute, Congress demonstrated its understanding of the difference between a drug and a dosage form or strength.

is greater than 34, the number of 30-day equivalent supplies is equal to the number of days' supply reported on each PDE divided by 30.²²⁰

CMS should further confirm that it will calculate the **total** thirty-day equivalent supply as the sum of individual thirty-day equivalent supplies across all applicable utilization of a selected drug.

- **Second, CMS should clarify how it intends to account for adjustments to PDE data in the calculation of the ceiling price and in the calculation of the dosage form/strength-level MFP.** PDE data may be adjusted until six months following the end of the plan year.²²¹ For IPAY 2026, the negotiation period will run from October 2, 2023, through July 31, 2024, such that the PDE data from the 2022 plan year will be finalized by the start of such period.²²² However, starting with IPAY 2027, the negotiation period will run from March 1 through November 1 of the year that is two years before the applicable IPAY. As PDE data for the preceding plan year will not be finalized until June 30 of such year, adjustments to such data will need to be accounted for when calculating the ceiling price and when applying the MFP across the dosage forms and strengths of the selected drug.
- **Third, CMS should clarify how it will calculate the twelve-month WAC used to calculate the dosage form/strength-level MFP.** We recommend that such WAC be a weighted average to accurately represent pricing across the twelve-month period. A weighted average would be consistent with CMS's general approach to calculating the ceiling price and to applying the MFP across the dosage forms and strengths of the selected drug, both of which rely on weighted averages.
- **Fourth, CMS's proposed calculations are incredibly complex; as such, CMS should provide numeric examples of how it intends to apply such calculations.** Numeric examples will enhance transparency and help stakeholders to understand CMS's proposed methodology.
- **Fifth, CMS should commit to provide each manufacturer of a selected drug with all of the PDE data on which CMS intends to rely under its proposed methodology.** Such data are not readily available to manufacturers and would be needed immediately upon selection for the MFP process to ensure that the manufacturer can meaningfully engage in such process.

B. Lilly Agrees with CMS That Manufacturers Should Be Permitted to Provide Access to the MFP Through an MFP Rebate Model

The statute grants CMS broad discretion to “establish[] . . . procedures to carry out the provisions of [the Program], as applicable, with respect to [MFP-eligible individuals].”²²³ Pursuant to this authority, the Guidance proposes that manufacturers may provide access to the MFP by either (1) ensuring that

²²⁰ 42 C.F.R. § 423.104(d)(2)(iv)(A)(ii).

²²¹ See, e.g., 2022 Annual PDE Data Submission Deadline, [https://www.csscoperations.com/internet/csscw3_files.nsf/F/CSSC2022%20Annual%20PDE%20Data%20Submission%20Timeline%20final_09%2022%202021.pdf/\\$FILE/2022%20Annual%20PDE%20Data%20Submission%20Timeline%20final_09%2022%202021.pdf](https://www.csscoperations.com/internet/csscw3_files.nsf/F/CSSC2022%20Annual%20PDE%20Data%20Submission%20Timeline%20final_09%2022%202021.pdf/$FILE/2022%20Annual%20PDE%20Data%20Submission%20Timeline%20final_09%2022%202021.pdf) (last accessed Apr. 6, 2023).

²²² SSA § 1191(d)(5); Guidance at 27, 55, 57.

²²³ SSA § 1196(a)(3).

the price paid when acquiring the drug is no greater than the MFP or (2) providing retrospective reimbursement for the difference between the drug acquisition cost and the MFP.²²⁴ This will allow for implementation of a rebate model, which is vital to ensure that the MFP is **exclusively** made available with respect to MFP-eligible individuals.

While Lilly agrees with the agency's approach of permitting access to the MFP to be provided through retrospective reimbursement, the reimbursement amount should be based on the difference between the MFP and WAC. WAC is the list price set and controlled by the manufacturer; manufacturers have no visibility into acquisition costs as wholesalers – which take legal title and physical possession of the product after it is shipped from the manufacturer's loading dock – are the sole arbiter of that price (except in those rare occasions where a manufacturer has an indirect contract with a pharmacy or provider).²²⁵

Also, as CMS knows, the statute requires that manufacturers provide access to the MFP only with respect to MFP-**eligible** individuals.²²⁶ Units of a selected drug purchased at the MFP therefore may not be administered or dispensed to individuals who receive benefits outside of the Part B, MA, or Part D programs, such as through a commercial health plan. Simply put, the plain terms of the statute effectively **bar** a provider or pharmacy from purchasing a unit of a selected drug at the MFP and dispensing it to an MFP-**ineligible** individual.

Despite this clear prohibition against MFP diversion, the statute does not provide manufacturers, or CMS for that matter, a right to audit providers and pharmacies for appropriate use of MFP units of selected drugs, and there is no statutory dispute resolution mechanism that manufacturers can use to recover MFP discounts from providers and pharmacies that administer or dispense MFP units to MFP-ineligible individuals. And there appears to be no statutory means at all by which CMS may penalize providers and pharmacies for administering or dispensing MFP-purchased units of selected drugs to MFP-ineligible individuals, such as by terminating a provider's or pharmacy's access to the MFP.

For this reason, a rebate model is **necessary** to effectuate the statutory prohibition against diversion of MFP units to MFP-**ineligible** individuals. By contrast, if the MFP were required to be offered only as an up-front discount at the time of purchase, it would be **impossible** to ensure that the provider or pharmacy subsequently administers or dispenses the unit to an MFP-eligible individual. Even if the manufacturer, or even CMS, were to subsequently ask the provider or pharmacy whether the unit was in fact appropriately administered or dispensed, it would have no means of recourse against the provider or pharmacy if the provider or pharmacy were to refuse to answer, or if the unit was in fact administered or dispensed to an MFP-eligible individual.

An MFP rebate model is the solution to this MFP diversion problem; rebate models are straightforward to administer, and a familiar construct already widely used in the Part D program and the commercial sector. Importantly, a rebate model will not jeopardize Medicare beneficiary access to reduced MFP-based cost-sharing. Providers and pharmacies will know at the time that a unit of a drug is administered or dispensed whether the drug is a selected drug and, if so, its associated MFP-based cost-sharing.

²²⁴ Guidance at 32.

²²⁵ In the event that the manufacturer provides a discount on the purchase price to the pharmacy or provider, that lower acquisition cost should replace WAC in the calculation of the reimbursement amount.

²²⁶ SSA §§ 1191(b)(2), 1193(a)(3).

For all of these reasons, Lilly strongly concurs with CMS's proposal to allow access to the MFP to be provided through an MFP rebate model, but encourages the use of WAC rather than acquisition cost.

C. To Make an MFP Rebate Model Meaningful, It is Vital That CMS Clarify That Rebates Are Owed Fourteen Days After the Manufacturer Has Verified MFP Eligibility

CMS proposes that manufacturers must furnish any retrospective reimbursement "within 14 days."²²⁷ The Guidance, however, does not specify when the fourteen-day clock starts to run.

It is imperative that CMS clarify that the clock begins to run on the day on which the manufacturer has **verified** that the individual to whom the unit of the selected drug was administered or dispensed was in fact an MFP-eligible individual. Starting the clock at any time before such verification occurs would be wholly irrational, as it would render the retrospective reimbursement model (i.e., rebate model) meaningless.

In addition, it is important that, to the extent the clock instead runs from the date on which all necessary validating Medicare claims data are received from the provider or pharmacy (in which case an additional fourteen days must be added to the clock to account for the need to validate MFP eligibility) and there is a dispute, the clock is tolled during the pendency of a reasonable dispute resolution process.

As explained in Section IX(B), a rebate model is necessary to effectuate the statutory prohibition against diversion of MFP units to MFP-**ineligible** individuals. The rebate model, however, is **only** useful to the extent it **actually** allows manufacturers to prospectively safeguard against the diversion of MFP units to individuals ineligible for the MFP. As such, a necessary prerequisite of a functional rebate model is that manufacturers not be required to pay rebates until **after** the manufacturer is able to verify that the rebate request relates to a unit of a selected drug that is actually eligible for the MFP. Even more fundamentally, there would be no incentive for the provider or pharmacy to furnish any Medicare claims data needed to validate MFP eligibility if a manufacturer were required to pay an MFP rebate within a specified time period, regardless of whether MFP eligibility has been validated. And, without a mechanism to ensure that a provider or pharmacy submits Medicare claims data and time for the manufacturer to verify MFP eligibility based on such data, any prospective safeguards afforded by a rebate model would become entirely illusory.

To this end, we recommend as an alternative that manufacturers be afforded 45 days from the receipt of all necessary validating data to pay the rebate to allow a reasonable window for processing as this is more consistent with commercial and Medicaid standards for rebate validation and payment. In other contexts, Congress has recognized that a longer window is appropriate for processing claims data. For example, section 1869(a)(2) of the SSA affords Medicare Administrative Contractors 45 days to evaluate whether a claim is clean – i.e., that it does not require further investigation or external development.²²⁸ In addition, to the extent that good faith disputes arise during processing, the clock should be tolled during that time such that manufacturers may withhold disputed rebate requests pending good faith resolution.

²²⁷ Guidance at 32.

²²⁸ SSA § 1869(a)(2); *see also* CMS, CMS Manual System: Pub 100-04 Medicare Claims Processing (Transmittal 1173), at 2, available at <https://www.cms.gov/regulations-and-guidance/guidance/transmittals/downloads/dwnlds/r1173cppdf.pdf>.

To give effect to Congress's prohibition of diversion of MFP units to MFP-ineligible individuals, we recommend that CMS specify that the rebate must be paid 45 days after the date on which the manufacturer receives all necessary validating Medicare claims data, and that the clock be tolled during the pendency of a reasonable dispute resolution process.

D. Lilly Concurrs with CMS That Manufacturers Should Not Be Required to Provide Access to the MFP to a Part D Beneficiary at the Point-of-Sale Directly

The statute provides that the manufacturer shall provide access to the MFP to Part D beneficiaries at the point of sale (as well as to pharmacies, mail order services, and other dispensers with respect to such individuals).²²⁹ In the Guidance, CMS correctly recognizes that, where units of a selected drug are dispensed to a Part D beneficiary, it would be **impossible** for **manufacturers** to provide the MFP at the point-of-sale **directly**.²³⁰ This is because manufacturers are **not** a party to the point-of-sale transaction. The point-of-sale transaction is instead among the pharmacy, the Part D beneficiary, and the plan (or its contracted pharmacy benefit manager (PBM)). Thus, the only logical way to effectuate the statutory mandate that manufacturers provide access to the MFP to Part D beneficiaries at the point-of-sale is by having the MFP discount passed through to such individuals by entities that **are** parties to the point-of-sale transaction. Therefore, we agree with CMS's clarification that access to the MFP by Part D beneficiaries must be effectuated through PD and MA-PD plans, and need not be directly provided by manufacturers.

E. CMS Should Work With HRSA to Enact Broad 340B Reforms Necessary to Implement the IRA and, at a Minimum, Should Require MA, MA-PD, and PD Plans to Require the Accurate Use of Either a 340B or Non-340B Claims Indicator for Part B and D Drugs as a Condition of Payment of a Claim for Reimbursement in Advance of IPAY 2026

Section 1193(d) of the SSA prohibits MFP-340B duplicate discounts.²³¹ By statute, manufacturers need only offer the lower of the two prices.²³² To effectuate Congress's intent in prohibiting MFP-340B duplicate discounts, CMS must adopt a mechanism to enable manufacturers to avoid paying such duplicate discounts on units of selected drugs – **including with respect to claims reimbursed by MA, MA-PD, and PD plans** – and should work with HRSA to undertake the host of broader 340B reforms necessary to ensure compliance with all of the recently enacted non-duplication provisions under the IRA.

To date, CMS has undertaken a weak and largely aspirational patchwork of reforms. For example, CMS has stated that, starting on January 1, 2024, all 340B covered entities that submit Part B claims must use specified 340B claims modifiers to identify 340B units.²³³ However, it is unclear what will happen to covered entities that fail to implement this requirement faithfully, nor has CMS identified any program integrity efforts (e.g., audits, exclusions, or penalties) that would drive covered entity compliance. With respect to Part D, CMS has similarly proposed to require use of a Part D 340B indicator as part of implementing the Part D inflation rebate program. In doing so, the agency acknowledged that “requiring that a 340B indicator be included on the [PDE] record is the most

²²⁹ SSA § 1193(a)(3)(A).

²³⁰ Guidance at 31.

²³¹ SSA § 1193(d).

²³² *Id.*

²³³ CMS, Part B Inflation Rebate Guidance: Use of the 340B Modifiers (Dec. 20, 2022), *available at* <https://www.cms.gov/files/document/part-b-inflation-rebate-guidance340b-modifierfinal.pdf>.

reliable way to identify drugs that are subject to a 340B discount that were dispensed under Medicare part D” for purposes of excluding 340B units from the Part D inflation rebate calculation.²³⁴

Lilly appreciates that these policies and proposals may constitute a reasonable starting point, but they fall short of ensuring that the clear statutory prohibition against duplicate discounts in the context of the Part B and Part D inflation rebate and MFP programs. Moreover, we have concerns that, where fraud or financial harm against a manufacturer is the policy concern, the government has been lax in deploying front-end controls and reluctant to impose back-end consequences. Accordingly, we urge CMS to work with HRSA to (1) define the statutory term “patient” for purposes of identifying and excluding ineligible 340B utilization; and (2) require covered entities to identify these patients at the point of drug administration or dispense.

In addition, there is a compelling need for the application of a consistent 340B claims indicator that applies across **all** types of claims, **including MA claims**, implicating the MFP-340B duplicate discount prohibition at the point of sale. Consistent and accurate use of a 340B claims identifier is **essential** to facilitate the prohibition of MFP-340B duplicate discounts. Absent such use of such an identifier, there is no means to identify units of drugs acquired under the 340B Program, and therefore no means to prevent MFP-340B duplicate discounts on selected drugs. We therefore strongly urge CMS to act expeditiously to mandate that MA, MA-PD, and PD plans to identify units of drugs acquired under the 340B Program using a consistent 340B claims identifier in their MA encounter data or PDE data.²³⁵ We recommend that CMS implement this policy via rulemaking. And accurate use of the applicable indicator should be made a condition payment of a claim for reimbursement.²³⁶ This is the case for **all** types of claims implicating the MFP-340B duplicate discount prohibition – i.e., Part B, MA, and Part D.²³⁷

It is paramount that CMS implement these policies given the well-documented history of improper duplicate discounting and Lilly’s own experiences. In the analogous context of MDRP-340B duplicate discounts, there is a long history of widespread 340B covered entity non-compliance with the MDRP-340B duplicate discount prohibition.²³⁸ Improper discounting persists despite statutory audit and dispute resolution processes and agency authority to penalize non-compliant 340B covered entities. By contrast, under the Program, there is no statutory audit or dispute resolution process to remediate MFP-340B duplicate discounts, nor any apparent agency authority to penalize a non-compliance provider or pharmacy.²³⁹ CMS must make certain that there are mechanisms in place to address this serious risk with respect to MFP-340B duplicate discounts. The statutory prohibition on MFP-340B

²³⁴ CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum 18 (Feb. 9, 2023), available at <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>.

²³⁵ The identifier used should be consistent where possible, though different identifiers may be used for MA encounter data versus PDE data (e.g., the former could use the JG/TB modifiers, whereas the latter could use a different CMS-designated identifier appropriate for pharmacy claim transactions).

²³⁶ For claims reimbursed under MA and Part D, CMS should impose a requirement on plans to make accurate use of the 340B or non-340B identifier a requirement of the plans’ reimbursement of the provider or pharmacy.

²³⁷ The need for a 340B identifier in MA is also not addressed in CMS’s existing policies on Part B claims involving units of drugs acquired under the 340B Program.

²³⁸ See, e.g., Government Accountability Office, Drug Discount Program: Federal Oversight of Compliance at 340B Contract Pharmacies Needs Improvement, GAO-18-480 (2018), available at <https://www.gao.gov/assets/gao-18-480.pdf>; see generally 42 U.S.C. § 256b(a)(5)(A).

²³⁹ Compare SSA § 1193(d) with PHSA § 340B(d)(3).

duplicate discounts is meaningful only if CMS establishes a reliable and consistent means to identify units of drugs acquired under the 340B Program.²⁴⁰

For all of these reasons, we urge CMS and HRSA to work together to ensure the broader 340B reforms necessary to implement all of the new requirements of the IRA and to, at a minimum, condition reimbursement for a unit of a selected drug on the accurate use of either a 340B or a non-340B claims indicator across Part B, MA, and Part D. Lilly also urges CMS to adopt these changes well in advance of the start of IPAY 2026, the first IPAY applicable to Part D drugs, and the start of IPAY 2028, the first IPAY applicable to Part B drugs, to enable a manufacturer to avoid paying MFP-340B duplicate discounts, as contemplated by the statute.

X. Other Considerations

A. CMS Should Clarify That Selected Drugs Are Not Subject to an Inflation Rebate

As part of soliciting comment on the interaction between inflation rebates and selected drugs,²⁴¹ CMS contends that “[t]he Part B and Part D inflation rebate programs apply to selected drugs, regardless of the status of the drug as a selected drug. Alternatively said, whether a drug is a selected drug will have no bearing as to whether the drug is also subject to the Part B and Part D inflation rebate programs.”²⁴²

CMS’s contention is troubling because it is untrue. Selected drugs are not subject to inflation rebates, and Lilly urges CMS to clarify that this is the case. Under the statute, the Part B inflation rebate calculation is based on the amount by which “106 percent of the amount **determined under paragraph (4)** of [section 1847A(b) of the SSA] for [a Part B rebatable drug] during the calendar quarter . . . exceeds . . . the inflation-adjusted payment amount . . . for such Part B rebatable drug during the calendar quarter.”²⁴³

Importantly, the circumstances under which an amount is “determined” under paragraph (4) of section 1847A(b) is dictated by section 1847A(b)(1).²⁴⁴ Section 1847A(b)(1) dictates a payment amount of, “in the case of a single source drug or biological . . . , 106 percent of the amount **determined under paragraph (4) of section 1847A(b) or** in the case of such a drug or biological product that is a selected drug . . . , with respect to a price applicability period . . . , 106 percent of the maximum fair price . . . applicable for such drug and a year during such period.”²⁴⁵

In other words, a selected drug’s payment **must** be determined under section 1847A(b)(1), and such payment amount must be determined **without regard to paragraph (4)** of section 1847A(b). Taken together, this means paragraph (4) defines the payment amount **only** for a **non-selected** drug. Accordingly, by statute, the Part B inflation rebate **cannot** be applicable to a selected drug – because there is no amount “determined under paragraph (4),” and therefore Part B inflation rebates cannot be applicable.

²⁴⁰ See SSA § 1193(d).

²⁴¹ Guidance at 71.

²⁴² *Id.*

²⁴³ SSA § 1847A(i)(3) (emphasis added).

²⁴⁴ See *id.* § 1847A(b)(1).

²⁴⁵ *Id.* § 1847A(b)(1)(B) (emphasis added).

There is also every reason to believe such outcome was intended by Congress. There is no policy reason for application of inflation rebates to selected drugs. The MFP **already** constrains Medicare expenditures for selected drugs, and thus it would be illogical Congress to apply inflation rebates in addition to the MFP.²⁴⁶ This is especially true because the MFP already shields Medicare from price increases outpacing inflation, which is the very situation that inflation rebates were designed to address. Accordingly, we ask that CMS clarify that a selected drug is not subject to an inflation rebate, consistent with both the language of the statute and sound public policy.

B. With Respect to CMPs, CMS Should Finalize Its Pre-Sanction Procedural Safeguards and Adopt an Additional Process Whereby Manufacturers Are Given Advance Notice of an Intent to Impose a CMP and a Reasonable Opportunity to Cure or Dispute the Deficiency, to Help Ensure That CMPs Are Imposed Only Where Appropriate

By statute, CMS must impose substantial CMPs on a manufacturer that is found to be non-compliant with certain program requirements.²⁴⁷ Specifically, if a manufacturer:

- fails to offer the MFP with respect to an MFP eligible individual, a penalty will be imposed equal to ten times the difference between the price paid and the MFP for each unit of the selected drug that is sold at a price above the MFP;
- violates the terms of the program manufacturer agreement, a CMP of \$1 million per day of noncompliance will be imposed;
- knowingly provides false information with respect to eligibility for the statutory exceptions provided for small biotech drugs and for biologicals where market entry of a biosimilar is highly likely, a penalty of \$100 million will be imposed for each item of false information; or
- fails to comply with rebate requirements with respect to a biologic where a delay in selection was granted but either (1) after a first year of delay, CMS determined that there was no longer a high likelihood that the biosimilar would launch within the specified timeframe or (2) after a second year of delay, the biosimilar did not timely launch, a penalty will be imposed equal to ten times the amount of the rebate the manufacturer failed to pay.²⁴⁸

In the Guidance, CMS states its intention to monitor compliance with the Program.²⁴⁹ And, where deficiencies are identified, the agency proposes to notify manufacturers of the basis for the CMP, the deadline to respond with a hearing request or pay the CMP (i.e., 60 days after the date of receipt of the CMP notice), and the amount due, among other things.²⁵⁰

Lilly supports CMS's proposal to provide manufacturers a CMP notice and a hearing to dispute the deficiency **before** imposing sanctions. We understand CMS's proposal to mean that, if a manufacturer requests a hearing to appeal a CMP, imposition of such CMP will be **stayed** pending resolution of such appeal.

²⁴⁶ *Id.* §§ 1847A(b)(1)(B); 1860D-2(d)(1)(D).

²⁴⁷ SSA § 1197.

²⁴⁸ *Id.* § 1197(a)–(e).

²⁴⁹ Guidance at 68–70.

²⁵⁰ *Id.* at 70.

Lilly concurs with this approach. Given that penalties could be in the hundreds of millions of dollars, it is critical that CMPs not be imposed while an appeal is still pending. Indeed, if CMS were instead to impose such massive penalties without any mechanism for pre-deprivation review, it would raise fundamental questions of due process.²⁵¹

Lilly also believes that additional pre-sanction procedural safeguards are needed to ensure that penalties are imposed only where appropriate. Specifically, Lilly strongly urges CMS to afford manufacturers at least **30 days advance notice of an intent to impose a CMP (i.e., 30 days before the date on which CMS would send the CMP notice) and an accompanying opportunity to cure or dispute any deficiency** based on a factual or legal error before imposing penalties.

An advance opportunity to cure or dispute is justified due to the novelty and the complexity of the MFP regime. There inevitably will be significant ambiguities with respect to program requirements, especially in the early years, which means that manufacturers will necessarily be seeking to comply with such requirement in a landscape of considerable uncertainty. The size of the penalties alone indicate that CMPs should be used as an enforcement tool only when clearly warranted by a manufacturer's substantial and continued noncompliance, and never for inadvertent oversights or minor mistakes. It would be fundamentally unreasonable to levy millions of dollars in CMPs on a manufacturer for failing to comply with a requirement on account of a technical mistake or misunderstanding where the manufacturer was seeking in good faith to comply with an ambiguously worded directive. Affording manufacturers an advance opportunity to cure or dispute is essential to the fair implementation of the Program.

C. CMS Should Exclude MFP Units from the Definition of "Unit" for Purposes of the ASP Calculation

Under the statute, the BP calculation includes MFP units.²⁵² And, generally speaking, sales included in BP are included in ASP.²⁵³ Thus, in the ordinary course, the inclusion of MFP units in the ASP calculation would progressively reduce ASP.

For Medicare fee-for-service (FFS) purposes, inclusion of MFP units in ASP does not affect reimbursement rates because selected drugs are not reimbursed on the basis of ASP. The same, however, is not true for **non-Medicare** FFS units of selected drugs. Non-Medicare FFS payers often rely on ASP as a benchmark to set reimbursement rates. As such, if MFP units are included in the calculation of ASP, ASP-based reimbursement rates of non-Medicare FFS payers will become increasingly insufficient to make providers whole for their acquisition cost of the selected drug.

To protect access to critical medicines in non-Medicare FFS markets, we urge CMS to amend its definition of "unit" for purposes of the ASP calculation to exclude MFP units. Unless CMS does so, there is a very real risk that providers may be unable to furnish selected drugs to MFP-eligible individuals because they cannot afford to do so.

There is clear legal authority for CMS to completely eliminate this risk by excluding MFP units from the ASP calculation. Notably, the ASP statute expressly delegates authority to CMS to make the

²⁵¹ See generally *Matthews v. Eldridge*, 424 U.S. 319 (1976) (factors for evaluating when due process requires a pre-deprivation hearing include the nature and magnitude of the private interest affected and the risk of an erroneous deprivation, along with any implicated governmental interest).

²⁵² SSA § 1927(c)(1)(C)(ii)(V).

²⁵³ *Id.* § 1847A(c); see also 42 C.F.R. § 414.804(a)(1), (4)(i).

recommended change to the regulatory definition of “unit.” Specifically, the statutory definition of “unit” authorizes CMS to “establish the unit for a manufacturer to report and methods for counting units as [CMS] determines appropriate”²⁵⁴ Further, the legislative history makes abundantly clear that the delegation of this authority was for the specific purpose of excluding “those sales that do not reflect market prices” from ASP, which MFP units, by definition do not.²⁵⁵

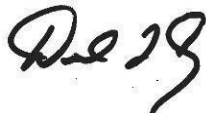
There is also clear regulatory precedent for excluding MFP units from the ASP calculation. CMS has excluded Competitive Acquisition Program (CAP) units from the ASP “unit” definition because ASP and CAP prices were “intended to be alternatives to each other.”²⁵⁶ Thus, CMS concluded that CAP units should be carved out from the ASP calculation.

The same logic applies here. The MFP is available only with respect to the Medicare FFS market.²⁵⁷ MFP-eligible individuals make up only a subset of the market, and, thus, the MFP does not reflect a market price that should be reflected in ASP in accordance with Congressional design. Moreover, the MFP, like the CAP, is an alternative to ASP, used in place of ASP to establish Medicare FFS reimbursement rates for Part B drugs that are selected drugs.

For these reasons, we urge CMS to exercise its authority to amend the ASP definition of “unit” to exclude MFP units from the ASP calculation.

Lilly appreciates the opportunity to comment on certain sections of the Guidance. We sincerely appreciate your thoughtful consideration of the issues discussed in this letter and look forward to working with you in the future to help ensure that patients have meaningful access to affordable health care benefits and prescription drug coverage. Please do not hesitate to contact Derek Asay at Asay_Derek_L@Lilly.com with any questions.

Sincerely,



Derek L. Asay
Senior Vice President, Government Strategy



Shawn O'Neil
Senior Vice President, Government Affairs

²⁵⁴ SSA § 1847A(b)(2)(B) (emphasis added).

²⁵⁵ See H.R. Rep. No. 108-391, at 587-88 (2003), *reprinted in* 1808 U.S.C.C.A.N. 1954-55.

²⁵⁶ 78 Fed. Reg. at 61,915.

²⁵⁷ SSA §§ 1191(c)(2)(A), (B); 1193(a)(1)(A), (B), (2)(A), (B).

APPENDIX A

CMS'S PROPOSED METHODOLOGY FOR APPLYING THE MFP ACROSS THE DOSAGE FORMS AND STRENGTHS OF A SELECTED DRUG	
Step 1: Cap the drug-level MFP at the lower of the two alternative drug-level ceiling prices.	
<p>Compare the MFP per thirty-day equivalent supply at the drug level to the lower of the two alternative ceiling prices, which are also calculated per thirty-day equivalent supply at the drug level</p> <ul style="list-style-type: none"> • If the MFP is higher than the lower of the two ceiling prices, reduce the MFP so that it is equal to the lower of the two ceiling prices²⁵⁸ • The result is an MFP per thirty-day equivalent supply at the drug level 	
Step 2: Calculate a weighted average WAC for each <i>dosage form and strength</i> of the drug per thirty-day equivalent supply, based on 2022 Part D PDE data. ²⁵⁹	
<p>STEP 2(a): Calculate the WAC at the NDC-9 level for each NDC-9</p> <ul style="list-style-type: none"> • Based on Part D PDE data for 2022: <ul style="list-style-type: none"> ◦ Divide total units for each NDC-9 by ◦ Total units for all NDC-9s of that dosage form and strength. • Multiply the result by • The WAC unit cost (reported by manufacturers and likely based on calendar year 2022 data) 	
<p>STEP 2(b): Calculate the weighted average WAC on the dosage form and strength level</p> <ul style="list-style-type: none"> • Sum the WAC unit costs for each NDC-9 as calculated in Step 2(a) 	
<p>STEP 2(c): Calculate average units per total 30-day equivalent supply at the dosage form and strength level</p> <ul style="list-style-type: none"> • Divide total units across all NDC-9s of a dosage form and strength by • The total 30-day equivalent supply for Part D data for 2022 	
<p>STEP 2(d): Calculate the weighted (by the NDC-9 ratio) average WAC per 30-day equivalent supply at the dosage form and strength level</p> <ul style="list-style-type: none"> • Multiply the result in Step 2(b) above by • The result in Step 2(c) 	
Step 3: Calculate a weighted average WAC for the <i>drug</i> per thirty-day equivalent supply at the drug level. ²⁶⁰	

²⁵⁸ Initial Guidance at 48.

²⁵⁹ *Id.* at 58 (Steps 1 through 4 of the application of the MFP process in the Initial Guidance).

²⁶⁰ *Id.* at 59 (Steps 5 through 7 of the application of the MFP process in the Initial Guidance).

<p>STEP 3(a): Calculate the ratio of the total 30-day equivalent supply for a dosage form and strength to the total 30-day equivalent supply across all dosage forms and strengths (i.e., on the drug level)</p> <ul style="list-style-type: none"> • Divide the total 30-day equivalent supply for each dosage form and strength by • The total 30 day equivalent supply across all dosage forms and strengths (i.e., the drug level)
<p>STEP 3(b): Calculate a weighted (by the 30-day equivalent supply ratio) WAC per 30-day equivalent supply on the dosage form and strength level</p> <ul style="list-style-type: none"> • Multiply the result from Step 3(a) for each dosage form and strength by • The result from Step 2(d) for each dosage form and strength
<p>STEP 3(c): Calculate the weighted (by the 30-day equivalent supply ratio) WAC per 30-day equivalent supply across all dosage forms and strengths (i.e., the drug level)</p> <ul style="list-style-type: none"> • Sum all the amounts calculated in Step 3(b) for each dosage form and strength
<p>Step 4: Calculate a WAC ratio for each dosage form and strength by dividing the weighted average WAC for each dosage form and strength, by the weighted average WAC for the drug.²⁶¹</p>
<p>Calculate the WAC ratio (i.e., the WAC per 30-day equivalent supply on the dosage form and strength level divided by the WAC per 30-day equivalent supply on the drug level)</p> <ul style="list-style-type: none"> • Divide the result from Step 2(d) by • The result from Step 3(c) <p>Note: If there is more than one dosage form and strength of the drug, at least one dosage form and strength will have a ratio that is greater than 1.0</p>
<p>Step 5: Derive a dosage form/strength-level MFP by multiplying the single drug-level MFP by the WAC ratio for each dosage form and strength.²⁶²</p>
<p>Calculate the MFP per 30-day equivalent supply on the dosage form and strength level</p> <ul style="list-style-type: none"> • Multiply the negotiated single MFP by the ratio in Step 4
<p>Step 6: Cap (a second time) the dosage form/strength-level MFP by comparing such MFP to the dosage form/strength-level ceiling price:</p>
<p>Compare the dosage form/strength-level MFP, as calculated in Step 5, to the applicable dosage form/strength-level ceiling price (calculated as part of determining the ceiling price at the drug level through as separate process). If the dosage form/strength-level MFP is higher than the applicable dosage form/strength-level ceiling price, reduce the dosage form/strength-level MFP so that it is equal to the applicable dosage form/strength-level ceiling price.</p>

²⁶¹ *Id.* (Step 8 of the application of the MFP process in the Initial Guidance).

²⁶² *Id.* at 59 (Step 9 of the application of the MFP process in the Initial Guidance).

Step 7: Calculate a per-unit dosage form/strength-level MFP per thirty-day equivalent supply on the unit level by dividing the result from Step 6 by the units per total thirty-day equivalent supply for the dosage form and strength.²⁶³

Calculate the MFP per 30-day equivalent supply on the unit level

- **Divide** the MFP per 30-day equivalent supply in **Step 6** by
 - The total number of units dispensed **divided by**
 - The total 30-day equivalent supply for a dosage form and strength

²⁶³ *Id.* at 59 (Step 10 of the application of the MFP process in the Initial Guidance).

APPENDIX B

Comments Related to Guidance Appendix C: Definitions for Purposes of Collecting Manufacturer-Specific Data

In this Appendix B, we provide our comments to CMS's proposed definitions for the purposes of collecting manufacturer-specific data found in Appendix C to the Guidance.

As a threshold matter, we highlight that the U.S. Securities and Exchange Commission (SEC) and other governmental bodies do not require external reporting of costs (including research and development costs) or profits at a product-specific level, and therefore Lilly does not prepare standard financial statements with this data at a product-specific level. Further, actual costs (including R&D costs) associated with individual Lilly products are not allocated, compiled, or reported by Lilly in the regular course of business, and estimated cost data (including R&D cost data) for individual products would reflect informal and unaudited financial analysis. Instead, Lilly produces audited financial reports on an enterprise level pursuant to governing regulatory standards and accounting principles. These audited annual reports are submitted to the SEC pursuant to federal laws and regulations.

As a result, Lilly believes manufacturers will need to make many reasonable assumptions for the purposes of calculating much of the data manufacturers will be required to submit to CMS. For manufacturers like Lilly, this data will be prepared solely for purposes of complying with the requirements of the IRA. Where possible, we recommend that manufacturer assumptions be based on existing audited financial reports submitted to the SEC and/or generally accepted accounting principles (e.g., U.S. GAAP).

Lilly has the following specific comments related to the definitions proposed in Appendix C of the Guidance.

Research and Development (R&D) Costs – General Comments

1. CMS Should Not Limit the Definition of R&D Costs to Costs Associated with “All FDA-Approved Indications of a Drug.”

CMS proposes allowing manufacturers to report R&D costs (pre-clinical, post-IND, etc.) “for all FDA-approved indications of a drug.” However, this proposal appears to ignore material costs incurred by manufacturers to invest in R&D for indications approved in non-U.S. markets (indications that may be approved by the U.S. FDA at a later time). Moreover, as we note elsewhere in our comments, this proposal is in tension with CMS's proposal to calculate “recoupment of R&D costs using the *global*, total lifetime net revenue for the selected drug.” The results of this recoupment calculation will be misleading, as a manufacturer will need to report global revenue (including revenue for indications approved in markets outside of the United States but that are *not* FDA approved), but the manufacturer will not be able to report the R&D costs associated with these approvals, which may be significant.

To resolve this tension and avoid this misleading result, CMS should allow manufacturers to submit global R&D expenses, regardless of whether a particular indication is FDA-approved.

2. CMS Should Define “Federal Funding” to Exclude “Indirect Federal Funding” and Should Allow Direct Federal Funding to be Allocated.

CMS is proposing to exclude “Federal funding” from the determination of R&D costs. CMS does not define “Federal funding,” and it is not clear from the Guidance whether CMS intends to exclude direct government funding of R&D, or direct and indirect funding. For example, the federal government may provide funding to a third-party entity or foundation that provides funding to manufacturers for R&D purposes. Because this indirect government funding may be unknown to manufacturers, we recommend that CMS exclude *indirect* Federal funding from the definition of “Federal funding.”

In addition, we highlight that Federal funding of preclinical research (like most preclinical research) is generally not product specific. As a result, such funding would need to be allocated, similar to how CMS acknowledges that indirect research costs must be allocated.

3. CMS Should *Include* Acquisition Costs in the Definition of R&D Costs.

CMS is proposing to exclude “acquisition costs” from the definition of R&D costs. This proposal ignores meaningful costs incurred by the manufacturer. Moreover, it is inconsistent with SEC guidance, which specifies that in-process R&D (IPR&D), including those IPR&D costs related to acquisitions, must be considered as normal costs of operations and included in Non-GAAP financial reporting as R&D costs. Specifically, in 2021, SEC clarified its position in letters to several manufacturers, including Lilly, that Acquired In-Process Research and Development (AIPR&D) should not be excluded from R&D expenses.

To comply with SEC’s guidance related to Rule 100(a)(2) of Regulation G, Question 100.01, beginning in 2022, Lilly included AIPR&D within non-GAAP EPS reporting. Thus, *excluding* such costs in a manufacturer’s reporting to CMS would be inconsistent with recent SEC statements on this matter and would ignore material costs. We recommend that CMS specifically include acquisitions costs in the definition of R&D costs.

4. CMS Should Not Exclude “Costs Associated with *Ongoing* Basic Pre-Clinical Research, Clinical Trials, and Pending Approvals” from the Definition of R&D Costs.

CMS is proposing to exclude “costs associated with *ongoing* basic pre-clinical research, clinical trials, and pending approvals” from the definition of R&D costs. We disagree with this proposal and believe excluding these costs ignores meaningful expenses incurred by manufacturers to advance and seek approval of innovative therapies. For example, manufacturers may continue to execute trials to further the understanding of approved molecules and to gain approval for additional indications of that molecule that will further benefit patients. However, these additional trial costs may be for indications that are not yet, and may not ever be, approved by FDA. We recommend that CMS specifically *include* these costs in the definitions of basic pre-clinical research costs, post-IND applications costs, etc., or specifically include these costs in the definition of “all other R&D costs.”

Moreover, as we note elsewhere in our comments, this proposal is in tension with CMS’s proposal to calculate “recoupment of R&D costs using the global, *total lifetime* net revenue for the selected drug.” The results of this recoupment calculation will be misleading, as a manufacturer will need to report global lifetime revenue (i.e., *ongoing* revenue), but the manufacturer will *not* be able to report global lifetime (i.e., *ongoing*) R&D expenses.

To resolve this tension and avoid this misleading result, we recommend that CMS specifically *include* ongoing R&D costs. Such approach better reflects not only the treatment of these expenses under U.S. GAAP but also results in a more proximate (and less misleading) recoupment calculation.

5. CMS Should Specifically Identify Milestone Payments As R&D Costs.

CMS is silent as to the treatment of milestone payments to third parties related to R&D (e.g., a payment paid based on achieving a Phase 1 or Phase 2 milestone). We recommend that CMS specifically clarify that milestone payments should be reported as R&D costs, consistent with recent SEC statements. In the absence of such clarification, we assume that milestone payments fit within the definition of direct research expenses, as such expenses can be specifically attributed to the discovery and preclinical or clinical development of the selected drug.

Research and Development (R&D) Costs – Comments on Specific Definitions

1. Definition 1 - R&D: Basic Pre-Clinical Research Costs: CMS Should Allow Manufacturers to Make Reasonable Assumptions Regarding Allocations of Research Expenses.

We agree with CMS's acknowledgement that manufacturers will need to proportionally allocate indirect pre-clinical research costs. We reiterate that manufacturers will need to make reasonable assumptions in their calculations and allocations of basic pre-clinical research costs.

2. Definition 2 - Post-Investigational New Drug (IND) Application Costs: CMS Should Specifically Allow Manufacturers to Make Reasonable Assumptions Regarding the Definition of Direct Costs for Post-IND Costs.

CMS proposes to define direct costs for post-IND costs as "Institutional Review Board (IRB) review and amendment costs, user fees, patient recruitment, per-patient costs, research and data collection costs, personnel, and facility costs that are directly related to conducting the dosing and Phase I, Phase II, and Phase III clinical trials during the post-IND period." We believe this definition could be construed too narrowly, as there are several trial-specific costs that are not specifically included in CMS's definition. For example, manufacturers incur costs such as clinical trial site monitoring, site training, safety stock, etc., that are essential to running clinical trials. Although some manufacturers may interpret these costs as "facility costs" or similar, we recommend that CMS specifically identify broader categories of direct expenses that are directly attributed to support of a clinical trial site, consistent with reporting of R&D expenses under U.S. GAAP and SEC reporting.

3. Definition 3 - R&D: Completed U.S. Food and Drug Administration (FDA)-Required Phase IV Trials: We Assume CMS Is Not Limiting Its Proposed Definition of Direct Costs for Completed Phase IV Studies to the Costs Listed in the Guidance.

CMS proposes to define direct costs for completed Phase IV studies to "*include* patient recruitment, per-patient costs, research and data collection costs, personnel, and facility costs that are directly related to conducting the completed Phase IV study" (emphasis added). We assume this definition *includes*, but is *not limited to*, these categories of costs. For example, there are many trial-specific costs (e.g., clinical trial site monitoring, site training, site contracting, safety stock, etc.) that are not

specifically identified in the Guidance. Consistent with our feedback to Definition 2 above, we recommend that CMS ensure its definition of “Completed FDA-Required Phase IV Trials” allows manufacturers flexibility to include categories of expenses that are directly attributed to support of a clinical trial site in a manner consistent with reporting of R&D expenses under U.S. GAAP and with SEC reporting.

4. Definition 4 - R&D: Post-Marketing Trials: CMS Should i) Further Clarify the Difference between Definitions 3 and 4, and ii) Broaden Definition 4 to Include Other Post-Marketing R&D Expenses, Including Expenses Not Associated with Clinical Trials.

As a threshold matter, we believe Definitions 3 and 4 may have some redundancy and could create confusion. Moreover, we believe there may be tension between CMS’s statement that R&D costs are costs associated with “FDA-approved indications of a drug,” but that Definition 4 may include “direct cost[s] for post-marketing trials conducted for the purposes of marketing claims.” We interpret this later statement to include such expenses as expenses related to post marketing studies related to new indications or line extensions, investigator-initiated studies, real-world evidence and/or observational studies, etc., that are not related to an approved indication, and that may not be related to a specific post-marketing clinical trial.

Accordingly, and consistent with our other comments, we recommend that CMS ensure this definition of Post-Marketing expenses allows manufacturers flexibility to include: i) categories of expenses that are directly attributed to support of a clinical trial site, and ii) other R&D expenses that may not be attributable to a clinical trial site (e.g., real-world evidence studies). This would be consistent with reporting of R&D expenses under U.S. GAAP and with SEC reporting guidance. In addition, we recommend CMS specify that this category may include expenses related to indications not approved, or not yet approved, by the FDA.

5. Definition 5 - R&D: Abandoned and Failed Drug Costs: CMS Should Broaden its Definition “Abandoned and Failed Drug Costs.”

We agree with CMS’s acknowledgement that manufacturers incur R&D costs associated with failed or abandoned products. However, CMS proposes limiting the reporting of such basic *pre-clinical research* costs to those costs associated with “the same active moiety / active ingredient or mechanism of action as the selected drug.”

We disagree with this limitation and believe it is overly narrow, as a large portion of basic pre-clinical research expense would not be assignable to any marketed product. For example, Lilly has made significant investment in researching Alzheimer Tau Tangle targeting molecules, some of which has failed, but all of which has contributed to the overall advancement of Alzheimer’s research. As a result, we recommend that CMS specially allow manufacturers to allocate the costs associated with abandoned or failed research to molecules in the same disease state or therapeutic class. This recommendation is consistent with CMS’s proposal to include in “failed or abandoned drug costs” an allocation of direct *post-IND costs*²⁶⁴ for drugs in the same therapeutic class as the selected drug that did not achieve FDA approval.

²⁶⁴ Similar to Definitions 2, 3, and 4, CMS has proposed that direct post-IND costs include IRB review and amendment costs, user fees, patient recruitment, per-patient costs, research and data collection costs,

6. Definition 6 - R&D: All Other R&D Costs: CMS Should Allow Flexibility in This Definition.

We appreciate that CMS has not adopted a definition for “all other R&D costs.” We assume that this category can include an allocation of indirect expenses, including R&D overhead expenses, non-molecule specific costs in support of research and trial development, and relevant general and administrative expenses that are not otherwise captured in the definitions above. (For example, CMS proposes to allow for an allocation of relevant general and administrative expenses in the determination of indirect research expenses associated with basic pre-clinical research.²⁶⁵ We assume an allocation of general and administrative expenses for other research, not pre-clinical, is appropriately captured in this Definition 6.)

In addition, manufacturers may classify certain expenses associated with Medical Affairs as R&D costs. We assume that certain Medical Affairs expenses directly associated with a product and classified as R&D costs should be included in this Definition 6.

Finally, as noted above, we recommended that Definition 4 be broadened to include other post-approval research and development expenses including or related to new indications or line extensions, investigator-initiated studies, real-world evidence and/or observational studies, safety monitoring, ongoing regulatory fees, and other post marketing R&D costs. To the extent CMS disagrees that these expenses should be captured in Definition 4, we assume these expenses would fit into this Definition 6.

7. Definition 7 - Global, Total Lifetime Manufacturer Net Revenue for the Selected Drug: CMS Should Resolve the Tension in Its Proposed Recoupment Calculation.

As noted elsewhere in our comments, CMS’s proposal to calculate recoupment using the global, total lifetime net revenue of the selected drugs is at odds with CMS’s proposed definitions of R&D expenses, both in terms of scope (*global* revenue versus expenses associated with *U.S. FDA* approvals) and in terms of timing (*lifetime* revenue versus expenses *excluding* ongoing or other lifetime expenses). As a result, and to better align with categorization of R&D expenses under U.S. GAAP and/or for SEC reporting purposes, we recommend that CMS specifically broaden the scope of R&D expenses to include global, lifetime expenses.

Current Unit Costs of Production and Distribution

As a threshold matter, we reiterate that the SEC and other governmental bodies do not require external reporting of costs at a product-specific level, and therefore Lilly does not prepare standard financial statements with this data at a product-specific level. As a result, Lilly believes

personnel, and facility costs that are directly related to conducting dosing and clinical trials for the drug. Consistent with our other comments, we recommend that CMS allow manufacturers flexibility to include in the allocation of post-IND costs categories of expenses that are directly attributed to the support of a clinical trial site in a manner consistent with reporting of R&D expenses under U.S. GAAP and with SEC reporting.

²⁶⁵ Similarly, CMS proposes to include “allocated shared operating and other indirect costs (such as capitalized production facility costs, benefits, generalized and administrative costs, and overhead expenses)” in the production and distribution costs.

manufacturers will need to make reasonable assumptions for the purposes of calculating the values required to be submitted, which may be prepared solely for purposes of complying with the requirements of the IRA.

1. CMS Should Define Distribution Costs to Include Additional Channel Fees and Expenses.

CMS proposes to define costs of distribution as all direct, and an allocation of indirect, costs related to “packaging and packaging materials; labeling; shipping to any entity (e.g., distributor, wholesaler, retail or specialty pharmacy, physician office or hospital, etc.) that acquires the drug from the Primary Manufacturer or any Secondary Manufacturer; and operating costs for facilities, transportation, and other expenses related to packaging, labelling, and shipping to any entity that acquires the drug from the Primary Manufacturer or any Secondary Manufacturer.” We note that manufacturers incur channel fees, including prompt pay discounts, administrative fees for inventory management and other wholesalers services, etc. These expenses are not explicitly called out in the Guidance, and they may be treated by manufacturers as a reduction in revenue, or as a distribution cost. Regardless, these expenses are important to understanding the totality of a product’s distribution costs, and we recommend that CMS include these expenses in the definition of distribution costs.

2. CMS Should Allow Allocation of Various Other Costs Associated with Producing and Distributing Product.

We agree with CMS’s recognition that manufacturers will need to allocate various direct and indirect costs. We recommend that CMS preserve flexibility in manufacturers’ ability to identify and allocate various product manufacturing costs in a manner consistent with U.S. GAAP and/or SEC reporting. Such costs may include expenses associated with royalties or other margin sharing arrangements, amortization of intangible assets, use/yield variances, purchase price variances, idle plant expenses, the impact of foreign exchange rate changes on inventories sold, etc. These expenses are part of standard U.S. GAAP accounting.

CMS should also factor in capital outlays required to build, improve, and/or maintain manufacturing facilities. While some of these costs may be reflected in the unit costs of production through depreciation expense, depreciation will not be representative of the significant capital investments required for entry and ongoing operations. CMS should carefully consider these investments when evaluating the total cost picture. In some product classes, there may not be alternative manufacturers with sufficient capacity given the significant barriers to entry.

Finally, CMS should consider the costs a new entrant would bear if they had to bring such a product to market and manufacturer the product at the same capacity as an incumbent manufacturer. This “replacement cost” is a better representation of the current benefit to society than costs in the past might have been.



April 14, 2023

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Sent via electronic mail

Re: Comments on *Medicare Drug Price Negotiation Program: Initial
Memorandum, Implementation of Sections 1191 – 1198 of the Social Security
Act for Initial Price Applicability Year 2026*

Dear Dr. Seshamani:

The EveryLife Foundation for Rare Diseases appreciates the opportunity to comment on the March 15, 2023 initial memorandum on the Medicare Drug Price Negotiation Program (MDPNP). The EveryLife Foundation was founded to empower the rare disease patient community and focuses on a range of public policy issues at both the federal and state levels. Ensuring every person with a rare disease or condition can obtain affordable access to any medication approved by the Food and Drug Administration (FDA) is a top priority.

The Foundation recognizes and appreciates the intent behind the prescription drug negotiation program established by the Inflation Reduction Act. We understand the frustration Congress and most Americans have with the high costs of prescription medications. But we also recognize that multiple factors contribute to the costs of prescription drugs and believe an effective solution will be informed by understanding the systemic cost drivers that impact the entire healthcare system as opposed to disproportionately focusing on any single sector. We urge policymakers to recognize the transformational impact many prescription medications have had on countless American lives, including the lives of those suffering from a rare disease or disorder, as well as their role in reducing or preventing costs in other areas of healthcare, such as inpatient admissions, as well immeasurable life years saved.

The EveryLife Foundation appreciates the opportunity to provide feedback on the implementation of the MDPNP. We recognize CMS was not required to solicit public input in this phase of implementation; however, the patient community remains concerned with the limited opportunities offered for stakeholder feedback given the timelines outlined in the March 15th guidance. We join with other patient advocacy organizations in calling for CMS to utilize official notice and comment opportunities as the MDPNP implementation continues.

Earlier this year, the rare disease community commemorated the 40th anniversary of the enactment of the Orphan Drug Act (ODA) into law. Before the ODA became law, there was little biopharmaceutical interest in developing medications for rare diseases. In the four decades since its enactment, the FDA has issued more than 1,100 orphan designated approvals to treat rare diseases and disorders. This is unquestionably a success story, but that work is far from finished. The stark reality is that even 40 years after the ODA, 95% of all rare diseases and disorders lack any FDA-approved treatment. And while the ODA turned a once barren landscape into a vibrant ecosystem, developing treatments for rare diseases remains a highly challenging pursuit.

We appreciate that Congress recognized, at least partially, the challenges associated with rare disease therapy development by excluding a product that is approved to treat a single rare disease or condition from the Medicare negotiations. While we believe that the exemption, as written, is too narrow, we are especially concerned that the interpretation of this exemption as laid out in the March 15th guidance is even more restrictive than Congress intended and will have a serious negative impact on any industry incentives to evaluate a potential second, third or further application of a rare disease drug to another disease or condition.

As a rare disease-focused organization, we are particularly concerned about the lack of opportunity to provide input into the criteria for determining eligible products for the initial price applicability year of 2026. Given the implications of the criteria for determining eligibility of some orphan products on the highly sensitive rare disease therapeutic development ecosystem, we have provided comments and requests for clarification for the agency's consideration.

Additionally, our comments focus on the following areas:

- **Orphan drug designated approvals vs designations when determining eligibility**
- **Broadening and Clarifying the Definition of Unmet Need**
- **Methods for Determining Clinical Benefit - Process for Identifying Therapeutic Alternatives, Comparators, Exclusion of QALYs, Patient Experience Data**
- **Communication and Engagement Throughout the MDPNP**
- **Ensure Timely Access to Therapies**
- **Beneficiary Outreach and Protections**
- **Implement a Robust Monitoring Program**

Application of the Orphan Drug Exemption – Clarifications to Preserve Orphan Drug Incentives

CMS should consider orphan drug designated approvals vs designations when determining eligibility

As CMS knows, seeking and receiving orphan designation for a candidate therapy is not the same as submitting an application for a therapy's approval. The former process typically occurs relatively early in the product development process, typically many years if not longer before any possible approval is granted. We urge CMS to explicitly state that a drug with an orphan designation will not lose its orphan drug exclusion simply if it applies for and receives a designation for a second orphan medication. In addition, we urge FDA and CMS to establish a clearly defined process for FDA to share updates with CMS on both designations and eventual approvals. Given the risks of therapy development, including in exploring the repurposing of a drug approved to treat one condition for efficacy in treating another condition, simply obtaining an orphan designation should not result in any changes to an orphan exclusion. We already know there is widespread off-label use of drugs to treat rare conditions and are

concerned that loss of the orphan drug exclusion upon granting of a designation rather than approval would only further exacerbate this problem. Therefore, we urge CMS to clarify this point and further clarify that the orphan drug exclusion under current law would only be lost if FDA approves the same drug for treating a second disease or condition.

CMS should clearly articulate how it will address rare disease drugs within the letter of the current law

We appreciate the point in the memorandum that *“CMS will use the FDA Orphan product designation database and approvals on the FDA website”* and urge further clarification of this intent. Clarity on how CMS plans to implement the orphan exclusion, including by explicitly stating how it will interpret the requirement that all approvals be within one disease area, is highly encouraged. With the advancements in personalized medicine, there has been an increase in drug development for specific mutations or subtypes of disease. We believe CMS should act within their authority under the law to clarify they will consider separate approvals for different mutations or subtypes of one disease as still eligible for the orphan drug exemption. Without this clarity there will likely be diminished willingness to invest in the additional clinical research necessary to demonstrate effectiveness for other components of the patient population, leaving healthcare professionals, patients, and payers without the evidence they need to make informed decisions about appropriate use.

There are several examples of approved products and those in the pipeline that demonstrate the importance of preserving the exemption if all approvals are within mutations or subtypes of one disease. For example, Kalydeco received its original orphan designation in 2006 and its first approval in 2012. The original approved label was for one CFTR mutation (G551D) for patients 6 years and above. Over the next ten years, it received ten additional approvals, addressing 37 unique gene mutations on the CFTR gene that can cause cystic fibrosis. With each successive approval, more and more patients, who once had few to no treatment options, were able to benefit from this first in class innovative treatment with the confidence that the drug was appropriate for them. Ongoing efforts to develop therapies for diseases like ALS, MPS and other genetic diseases may face similar trajectories; and if not clarified, CMS risks negatively impacting the likelihood of these programs reaching the full range of potential eligible patients.

CMS should identify potential impacts related to changes in formulation

We urge CMS to clarify how the agency will address a potential situation in which a sponsor puts forward a new formulation that is clinically superior compared to the original formulation. The first-generation unity recognizes that first generation therapies may often be limited in their overall efficacy. But it is our hope that through further research, development, and exploration, product developers will produce more efficacious second, third, and subsequent generation treatments, including superior formulations of a first-generation product. We urge CMS to articulate how, for the purposes of IRA implementation, it plans to treat instances in which it determines that a new formulation warrants a product’s designation as a new molecular entity.

CMS should address combination therapies involving one or more rare diseases:

We encourage CMS to state how the agency will address medications that are a combination of two products. For example, if one of the two products is approved to treat a second orphan drug, how would that impact the exclusion for the combination product?

Factors Relevant to the Determination of Maximum Fair Price

Broadening and Clarifying the Definition of Unmet Need

Though we appreciate the guidance defined an unmet need as “treating a disease or conditions in cases where very limited or no other treatment options exist,” we urge CMS to clarify how it defines *limited treatment options* and how it will determine unmet need overall. A too narrow definition runs the risk of disincentivizing further therapy development in a space that still requires additional treatment at the risk of not meeting the unmet need exemption. Often within the rare disease space, drugs will be approved that only address one aspect of a condition or one specific mutation that can cause the disease or may be intended to slow disease progression but is not curative. A too narrow definition that does not take into account how treatments are utilized runs the risk of stunting interest in finding new and better treatments for the community.

Methods for Determining Clinical Benefit - Process for Identifying Therapeutic Alternatives, Comparators, Exclusion of QALYs, Patient Experience Data

We appreciate CMS’s thoughtful considerations on the identification of therapeutic alternatives and the several points raised related to our rare disease community’s priorities.

With respect to the identification of *Indications for the Selected Drug and Therapeutic Alternatives for Each Indication (60.3.1)*, CMS has stated that therapeutic alternatives for each indication of the selected drug will be considered. CMS has further stated that it “*considered evaluating non-pharmaceutical therapeutic alternatives; however, for initial price applicability year 2026, the agency plans to only consider therapeutic alternatives that are covered Part D or Part B drugs or biologics. CMS believes that pharmaceutical therapeutic alternatives will be the most analogous alternatives to the selected drug when considering treatment effect and price differentials.*” We concur that pharmaceutical alternatives are most appropriate comparators of the selected drugs and urge CMS to make permanent the consideration of only pharmaceutical therapeutic alternatives. In addition, we ask CMS to not consider *drugs* approved for each indication to be appropriate comparators to *biologics* within the same indication.

Related to the analysis of *Selected Drugs with Therapeutic Alternative(s) (60.3.3)*, we are appreciative of CMS’ emphases on the products’ outcomes and safety profiles.

We applaud CMS’ exclusion of metrics that treat extending the life of any individual as lower value than the life of another individual; this includes QALYs when used in association with life extension. Evidence that values extending the lives of some as less than extending the lives of others, whether based on disability status, age, diagnosis, demographic, or special populations, is unethical. We appreciate that CMS is seeking input on what other measures should also be considered inappropriate, and equally as important, which measures should be considered appropriate for use.

In addition to the outcomes listed by CMS for consideration (safety, efficacy, health outcomes, intermediate outcomes, surrogate endpoints, patient-reported outcomes), we suggest that CMS consider measures that are seen as beneficial to patients and caregivers¹. Those include measures that capture direct medical costs, especially out-of-pocket costs; non-medical costs to patients and families, effects on future costs, and work loss and absenteeism. The National Economic Burden of Rare Disease Study estimated the overall annual economic burden of rare disease in 2019 exceeded \$966 billion in the United States. Of the total economic burden, the largest costs were indirect costs from productivity losses at \$437 billion, direct medical costs at \$418 billion and non-medical and uncovered healthcare costs of \$111 billion absorbed directly by families living with rare diseases. Aside from absenteeism, inpatient care was the biggest expense, accounting for nearly 15% of the overall economic burden while prescription medication and administration costs accounted for about 10% and outpatient care for about 6%. Meaningful assessments of product affordability must focus on more than just one aspect of the overall health care system².

As the science of Patient-Focused Drug Development has evolved beyond the regulatory ecosystem, several organizations and initiatives have served as leaders within this space. To that end, CMS should work closely with patient communities, as well as partners such as the Innovation and Value Initiative (IVI), the National Health Council (NHC), the Institute for Gene Therapies (IGT), PAVE (the Patient Driven Values in Healthcare Evaluation) within the University of Maryland School of Pharmacy, and other leaders within this space who are leading innovative, patient-centered valuation efforts.

Communication and Engagement Throughout the MDPNP

We appreciate the agency's interest in creating a useful public explanation for the negotiated MFP. There is a great deal at stake for the rare disease community and a clear understanding of what factors were considered in determining the MFP is necessary to guide ongoing stakeholder engagement and clarity to the investment community that catalyzes most rare disease therapy development. As communities, we have evolved our engagement within the neighboring product development and regulatory ecosystems and have developed processes that enable engagement, patient experience data inclusion, and transparency.

While fewer than 5% of the more than 10,000 rare diseases have any FDA-approved disease-modifying therapies, we are grateful for recent breakthroughs that have extended the life expectancies of once-fatal conditions and we are optimistic about the research that is ongoing to develop treatments for additional conditions. For more than a decade, the rare disease patient community has played a significant role in the paradigm shifts and statutory changes that have occurred with respect to the inclusion of patients and patient experience data within clinical trial design, product development, and regulatory review.

As collaborative stakeholders, we have experienced a tremendous evolution of patient engagement and related areas since their infancy in PDUFA V – through their continued development via the 21st Century Cures Act and PDUFA VI -- and now their continued maturation in the implementation of PDUFA VII today. In this time, the landscape has shifted for the rare disease community. We've seen a deepened engagement and understanding of the patient perspective via numerous approaches such as through the evolution of Patient Focused Drug Development that facilitated new levels of transparency and engagement between regulatory agencies and relevant stakeholders around the integration of patient experience data within the regulatory review.

As a positive byproduct of these engagements, the CDER-issued [series of guidance documents](#) for conducting patient-focused drug development have been critical tools in providing stakeholders with practices for

- collecting comprehensive and representative input;
- methods to identify what is important to patients;
- selecting, developing, or modifying fit-for-purpose clinical outcome assessment; and,
- incorporating clinical outcomes assessments into endpoints for regulatory decision-making.

In addition, FDA’s issuance of numerous other guidances has been critical to our pipeline as it has informed the inclusion of patient experience data within clinical trial and patient-focused product development activities for drugs, cell- and gene-based therapies, diagnostics, and medical devices.

We encourage CMS to leverage the lessons learned throughout the evolution of patient focused drug development experiences in the regulatory environment as it proceeds with MDPNP implementation, including the proposed communication and transparency restrictions and in the required public explanation.

Gag Period Implications

Frequent and open communication before, during, and after the negotiation process is paramount to establishing public trust in the process and to informing the evolution of a program that constitutes a significant change in how drug prices are determined. Unfortunately, the restrictions proposed in Section 40.2.2 are likely to result in decreased transparency and reduced ability to understand and address the lessons learned in each negotiation process. While we understand and appreciate the need to protect the confidentiality of certain proprietary business information, imposing what amounts to a “gag order” on manufacturers is counterproductive. We encourage CMS to adapt the intended communication restrictions to prohibit sharing of only the most sensitive proprietary information and to abandon plans to place blanket restrictions on the sharing of information exchanged during the negotiation process. We hope CMS leverages its experience on how to communicate agency interactions and sensitive information within the regulatory environment to inform a final plan for what information will be restricted.

Content for Public MFP Explanation

To be an effective engagement tool, we encourage CMS to consider the following elements:

- Stakeholder groups who were engaged during negotiation
- Whether patient experience data (PED) and real-world evidence (RWE) was submitted during the negotiation process
- If patient experience data (PED) and real-world evidence (RWE) was considered in determining the MFP
- If submitted information was not considered to be relevant, publish a discussion of the rationale including what limited the agency’s ability to consider the submitted information
- Which metrics were used to evaluate clinical benefit
- Which outcome measures were considered when selecting therapeutic alternatives
- Criteria used to determine unmet need

The final public explanation must be easy to navigate and while much of the requested information is technical in nature, we encourage CMS to provide an appropriate short summary that will enable patients to understand the process that was used to determine the MFP and what they can expect to experience when obtaining their negotiated product. Additionally, while we recognize CMS is not statutorily required to publish the public explanation prior to March 1st of the year prior to the IPAY, we urge the agency to consider moving up this timeline to ensure that the information obtained in the explanation can be used by stakeholders to inform the submission of information for the selected products in the next IPAY.

Ensure Timely Access to Therapies

We appreciate that the law requires payers to include products selected for the MDPNP on the plan formulary. Rare disease patients are facing an onslaught of restrictive coverage policies, high cost-sharing requirements, and burdensome utilization management strategies. While the requirement to include the negotiated product on the formulary is a step in the right direction, we urge CMS to provide additional clarity on the parameters for coverage of negotiated products. Such parameters should seek to provide fair access to negotiated products and limit the potential for payers to arbitrarily implement restrictive utilization management practices as a reaction to increased liability because of the Part D redesign component of the IRA or as a reaction to the required coverage. It is also essential that CMS clarify that plans should not place additional utilization management restrictions on non-negotiated therapeutic alternatives solely due to their negotiation status.

Beneficiary Outreach and Protections

The MDPNP represents a significant technical change to how some drug prices are set, however much of this process is occurring outside of the view of the average Medicare beneficiary. We believe it is important for CMS to consider previous learnings from large scale program implementation efforts, such as the implementation of the durable medical equipment competitive bidding program, when designing beneficiary education and protection efforts. For example, we appreciate the intention to establish a toll-free number and email as mentioned in section 90.2; however, without sufficient public awareness and understanding of what eligible individuals are entitled to and the complaint mechanisms that exist, these resources will go under-utilized. We suggest that CMS consider identifying opportunities to include clear and accessible information about access to the MFP for negotiated products and complaint mechanisms in highly visible locations that don't rely on a beneficiary seeking out said information online or a third party remembering to provide such information. Considerations could include placement on leaflets provided by retail pharmacies with each prescription, along with additional placements in patient portals, relevant healthcare professional locations and community settings.

Implement a Robust Monitoring Program

The rare disease therapeutic development ecosystem is highly sensitive to changes in policy and the underlying incentives that drive investment in high-risk and high unmet need communities. For this reason, the [Rare Disease Community Statement on Drug Pricing Policy Priorities](#) recommends that rare disease therapies are excluded from policy experiments or demonstrations that significantly alter how prices are set until or unless it is proven that the changes do not threaten patient access and medical innovation. Given the limited nature of the exclusion for orphan drugs in the MDPNP, active monitoring

of a broad range of metrics to monitor the impact of the program on the rare disease ecosystem is paramount.

Specifically, we suggest CMS establish procedures to monitor the following metrics:

- Increases in launch price trends
- Growth in the use of utilization management strategies
- Trends in the approval of new indications for approved orphan designated products
- Increased time between completion of phase 3 clinical trials and FDA filing for follow on indications of approved orphan designated products
- Trends in the approval of new formulations of approved products
- Shifts away from investment in drug development programs for rare diseases that primarily affect Medicare beneficiaries
- Reliance on off-label use of therapies

Actions CMS can take to Support Orphan Drug Development

Beyond clearly articulating how the agency plans to interpret the statutory language and preventing any overly narrow approach to implementation, we appreciate CMS' interest (as stated in section 30.1.1) in other actions it could take to support orphan drug development. With that in mind, and recognizing these actions are outside of the scope of the current MDPNP, we offer the following points for the agency's consideration.

- **Support early dialogue between payers and rare disease developers/ manufacturers:** The FDA has long operated a program that provides medical device manufacturers with the opportunity to engage with payers early in the development process to obtain payer feedback that may inform clinical evaluation and other decisions. The intent is to maximize the likelihood of favorable coverage policies upon a product's market clearance. The EveryLife Foundation sees tremendous value in this approach and believes FDA and CMS should institute a similar program focused on rare disease therapy development which falls under the authority of CDER and CBER. Through a rare disease early payer engagement program, CMS and FDA can jointly establish a process to enable voluntary early dialogue between rare disease product manufacturers and payers – including Medicare and Medicaid. Through such interactions, we would hope that payers could provide invaluable inputs, including thoughts on trial design and data needs they will want to see to support a positive coverage decision. These interactions would also help manufacturers educate payers about specific rare diseases and conditions as well as the impact an approved therapy would have on the patient population. Given the potential significant benefits associated with an early payer engagement program, we urge CMS to work with FDA to launch such an initiative in the near-term.
- **Support development of diagnosis codes for rare diseases and disorders.** The diagnostic odyssey is the term used to describe the often multi-year period – and the rounds of medical appointments, tests, and other procedures – that patients with rare disease must often navigate just to receive an accurate diagnosis. One of the challenges associated with this process is the lack of ICD-10 codes for rare diseases and conditions. CMS, along with the Centers for Disease Control and Prevention (CDC) plays an important role in this process by staffing the ICD-10 Coordination and Maintenance Committee, which handles requests for new or updated codes. Some rare disease communities have been successful in navigating the process to successfully

develop codes for their disease or condition, but the vast majority of rare diseases lack any such codes. We would encourage CMS to work with the CDC to identify and implement improvements to facilitate the promulgation of additional rare disease codes. Specifically, we would encourage them to work on resource guides to help patient communities and researchers understand and navigate this process. In addition, convening a dedicated meeting or meetings of the committee each year focused on rare disease applications should be considered. Ultimately, by establishing more diagnostic codes for rare diseases, CMS can help shorten the diagnostic odyssey and could also help enhance understanding of a rare disease's natural history.

- **Do not Undermine FDA approvals and create additional impediments to coverage.** The Foundation is concerned about actions CMS has taken that have hindered program beneficiary access to FDA-approved medications, demonstrated most clearly in the agency's actions regarding novel therapies for Alzheimer's disease. While Alzheimer's is not a rare disease, we are troubled by the actions that have cast dispersion on the validity of an approval pathway created by Congress and of high importance to rare disease stakeholders. Limitations in natural history data associated with many rare diseases necessitate the use of a validated surrogate endpoint. We recognize the concerns regarding how the approval pathways have at times been used and the desire of policymakers to address these gaps. But, we are very concerned about actions that threaten to undermine the pathway overall and the ramifications such actions may have for those developing therapies to treat rare conditions and, most importantly, the patients who stand to benefit. We urge CMS to clearly recognize and communicate the value of the Accelerated Approval pathway which has been so successfully applied for patient unmet needs in common and rare cancers and to prevent from taking any actions that undermine drugs approved via this pathway. Specifically, we urge you to ensure that any rare disease therapy approved under Accelerated Approval be fully covered by programs under your authority.
- **Innovate in Utilization Management Strategies**
In rare diseases, time is a precious commodity. Extensive diagnostic odysseys often lead to diagnoses of rapidly progressive diseases with limited life expectancies. Utilization management techniques create unnecessary hurdles to critical and time-sensitive treatment interventions, yielding irreversible disease progression and catastrophic healthcare costs.

In 2021, 94% of prior authorization requests were approved, but of the over 2 million requests that were denied, only 11% were appealed with only 80% of those being successfully appealed. The data aligns with the stories we consistently hear from rare disease patients³. We urge CMS to partner with CMMI to explore innovative ideas to radically change the use of prior authorization policies, especially for vulnerable populations including those with rare diseases. Gold carding programs, shortened response times, and creating a pathway to eliminate prior authorization for certain drugs are among the many ideas that would help to limit the amount of prior authorization requests submitted for vital treatments and services.

Conclusion

Lowering the cost of health care, including prescription drug therapies, is an important goal that warrants thoughtful insight on how best to develop policies that will ensure the lowering of costs while

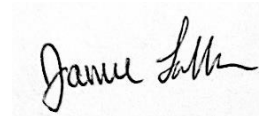
limiting potential negative unintended consequences. Policies that are implemented without consideration of the impact on incentives for rare disease research and development will mean lives will be lost and unnecessary suffering will be extended. We appreciate CMS's thoughtful process to ensure that the proposed negotiation process does not harm the same patients it is intending to help.

Thank you for the opportunity to provide comments on how the proposed negotiation process could impact the rare disease community and potential avenues to ensure that rare disease therapy development is not harmed through that process; the EveryLife Foundation and our partners are eager to engage with you. Please contact Jamie Sullivan, Senior Director of Policy at jsullivan@everylifefoundation.org if we can provide any additional information to inform your process.

Sincerely,



Annie Kennedy
Chief of Policy, Advocacy, & Patient Engagement
EveryLife Foundation for Rare Diseases



Jamie Sullivan
Senior Director of Policy
EveryLife Foundation for Rare Diseases

CC: Julia Jenkins, Executive Director
Frank Sasinowski, Chair, Board of Directors
Vicki Seyfort-Margolis, Vice-Chair, Board of Directors

Citations

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April 14, 2023

BY ELECTRONIC FILING (IRAREbateandNegotiation@cms.hhs.gov)

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**RE: Medicare Drug Price Negotiation Program: Initial Memorandum,
Implementation of Sections 1191 – 1198 of the Social Security Act for Initial
Price Applicability Year 2026, and Solicitation of Comments**

Dear Deputy Administrator Seshamani:

Exelixis is writing to submit comments on the Centers for Medicare & Medicaid Services' (CMS) initial guidance regarding the Drug Price Negotiation Program (Program) under the Inflation Reduction Act of 2022 (IRA) (Initial Guidance).¹

Exelixis is an innovative, research-based pharmaceutical company that focuses exclusively on accelerating the discovery, development, and commercialization of new medicines for difficult-to-treat cancers. We are committed to serving patients in desperate need of more effective cancer therapies. Our discovery efforts have resulted in two available products that are marketed by Exelixis: CABOMETYX® (cabozantinib) tablets and COMETRIQ® (cabozantinib) capsules. Exelixis has a long-standing commitment to research and development (R&D), year-over-year making significant investments to deliver the next generation of medicines that raises the standard of care for patients with cancer. Before we had a commercialized product, we spent between 73 percent and 87 percent of operating expenses on R&D (nearly \$2.3 billion). In 2022, Exelixis invested approximately 55 percent of its revenue for the year in R&D, and we anticipate investing approximately 56 percent of our revenue in R&D in 2023.²

¹ CMS, Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (Mar. 15, 2023), *available at* <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

² Exelixis Announces Fourth Quarter and Full Year 2022 Financial Results and Provides Corporate Update (Feb. 7, 2023), *available at* <https://ir.exelixis.com/news-releases/news-release-details/exelixis-announces-fourth-quarter-and-full-year-2022-financial>.

We are incorporating by reference comments from our trade association (BIO) and commenting here on issues of particular importance to Exelixis. Exelixis' comments can be summarized as follows:

- Consistent with the statute, CMS cannot require manufacturers to provide access to the maximum fair price (MFP) to individuals who are not MFP-eligible. Therefore, CMS should not require manufacturers to provide access to the MFP until after the manufacturer verifies that an individual is MFP-eligible. Exelixis recommends that CMS designate a centralized third-party administrator (TPA) to facilitate retrospective MFP discounts. Following the TPA's initial verification, Exelixis recommends that the TPA provide manufacturers with access to claims-level data, which would enable manufacturers independently to verify whether an individual is eligible for an MFP discount. Exelixis further recommends that CMS define the MFP discount based on the difference between the MFP and the annual non-Federal average manufacturer price (ANFAMP), rather than a pharmacy's actual acquisition cost.
- CMS should establish mechanisms to prevent duplicate 340B and MFP discounts, consistent with the Agency's statutory obligation. At a minimum, Exelixis recommends that CMS: (a) require covered entities to use 340B claims indicators and reject claims that do not include the proper indicator; (b) leverage the TPA to verify the 340B status of selected drugs; and (c) include the 340B indicator in the claims-level data that the TPA provides manufacturers, so that manufacturers also can verify the 340B status of a selected drug. In order to further reduce the risk of duplicate discounts, Exelixis encourages the Agency to permit manufacturers to provide the 340B ceiling price as a retrospective rebate, after an individual's eligibility has been verified.
- Consistent with Congressional intent, CMS should implement the carveout for small biotech drugs in a manner that protects small and mid-size biotechnology companies, which are the engines of discovery. Accordingly, CMS should make clear that pursuant to the definition of qualifying single source drug set forth in the Initial Guidance—under which all dosage forms, strengths, and formulations that share the same active moiety and the same New Drug Application (NDA) holder are considered together—a qualifying single source drug must qualify as a small biotech drug for *all* of its formulations, provided the NDA holder retains ownership of these formulations (and thus they continue to constitute the same qualifying single source drug).

I. CMS Should Establish Mechanisms to Ensure that the MFP is Provided Only to Eligible Beneficiaries

Under the IRA, a manufacturer of a Part D selected drug must agree to provide access to the MFP to “[MFP]-eligible individuals . . . at the pharmacy, mail order service, or other dispenser at the point-of-sale of such drug” and to such individual’s “pharmacy, mail order service or other dispenser.”³ In relevant part, an “[MFP]-eligible individual” is defined as “an individual who is enrolled in a prescription drug plan under part D of title XVIII or an MA-PD plan under part C of such title if coverage is provided under such plan for such selected drug.”⁴ Significantly, the statute does not require manufacturers to provide MFP access to an individual who is not an MFP-eligible individual.

The Initial Guidance states that manufacturers may provide access to the MFP in one of two ways: “(1) ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP; or (2) providing retrospective reimbursement for the difference between the dispensing entity’s acquisition cost and the MFP.”⁵ The Initial Guidance further states that a manufacturer that chooses to provide access to the MFP through retrospective reimbursement must reimburse “pharmacies, mail order services, and other dispensers, as well as intermediary entities, such as wholesalers, as applicable . . . the full amount of the difference between the acquisition cost for the selected drug and the MFP within 14 days.”⁶

A. Manufacturers Should Not be Required to Provide Access to the MFP Until After Verifying that an Individual is MFP-eligible

Exelixis supports permitting manufacturers to provide the MFP via a retrospective discount. As described in the comments of our trade association, BIO, the lack of any statutory audit or enforcement mechanisms against dispensers makes it vital that manufacturers be able to verify that an individual is MFP-eligible before providing the MFP discount. However, we are concerned that the Initial Guidance does not explain how CMS (or manufacturers) will be able to verify whether an individual is eligible for the MFP. This is critically important because the statute does not require manufacturers to provide access to the MFP to individuals who are not MFP-eligible. Therefore, as a matter of program integrity, Exelixis urges CMS to establish a transparent, centralized mechanism that will allow manufacturers to verify that an individual is MFP-eligible before the manufacturer is required to provide an MFP discount.

Exelixis disagrees with CMS’s suggestion in the Initial Guidance that wholesalers could help facilitate MFP discounts. In relevant part, the Initial Guidance states:

³ Social Security Act (SSA) § 1193(a)(3).

⁴ SSA § 1191(c)(2).

⁵ Initial Guidance § 40.4.

⁶ Initial Guidance § 40.4.

For example, a pharmacy may purchase a medication for \$100 per bottle and the MFP as applied to this selected package is \$80. The Medicare beneficiary is enrolled in a Part D plan under which coverage of the selected drug is available, thus the beneficiary is an MFP-eligible individual. For this example, the plan has not negotiated a lower price for the medication. The pharmacy provides the negotiated price (i.e., MFP plus a dispensing fee) at the point of sale to the Medicare beneficiary. As a result of this transaction, the pharmacy is owed \$20 by the manufacturer. The pharmacy would submit the information regarding the \$20 chargeback amount to its wholesaler and receive a credit from the wholesaler for that amount. The wholesaler would be compensated by the manufacturer after billing the manufacturer for the chargeback amount.⁷

Wholesalers are not well-positioned to oversee effectuation of the MFP. Wholesalers do not engage in claims-level transactions with pharmacies, and therefore do not have access to the data needed to verify whether an individual is MFP-eligible. In addition, there are dozens of wholesalers in the nation, making it difficult to create any sort of standardized claim verification and payment process through the wholesaler channel. In particular, smaller regional wholesalers may be unable or unwilling to collect and provide the information necessary to verify MFP discounts, which could cause further consolidation in the drug distribution system and imperil drug access in portions of the country, such as rural areas, that are serviced by regional wholesalers.

Instead, Exelixis recommends that CMS designate an independent, centralized TPA to facilitate retrospective MFP discounts. This entity could serve a similar role as the TPA in the Medicare Part D Coverage Gap Discount Program, which identifies claims eligible for discounts and facilitates the transfer of funds between pharmaceutical manufacturers and plan sponsors. The TPA model has proved workable in appropriately handling claims-level data, resolving disputes by manufacturers, and processing invoicing and payments from manufacturers in a timely manner.

After the TPA screens claims to determine if the individual is MFP-eligible, the TPA should provide manufacturers with access to certain claims-level data elements from the Prescription Drug Event (PDE) record, so that the manufacturers are able to verify whether an individual is MFP-eligible. At a minimum, manufacturers would need access to the following fields from the PDE record: national drug code (NDC), drug description, Rx ID, billing code, 340B indicator (discussed below), dispense/service date, dispensing/ provider national provider identifier (NPI), dispensing pharmacy/ provider name, pharmacy claim ID, prescribing NPI, dispensed units, billed units, billed amount, reimbursement amount, submission date, claim date, and Medicare plan ID.

Finally, Exelixis believes that 14 days — even if measured from the date of the manufacturer's receipt of complete claims information — is not sufficient time for manufacturers

⁷ Initial Guidance § 90.2.

to verify that an individual is MFP-eligible. Manufacturers should have time commensurate with industry standards before they are required to pay the MFP discount. For example, manufacturers have 38 days after receiving an invoice to pay a discount under the Part D Coverage Gap Discount Program,⁸ and 37 days to pay a rebate after receiving a rebate invoice under the Medicaid Drug Rebate Program.⁹ A period at least this long would be appropriate for verification of the MFP, which involves complex determinations of whether an individual is MFP-eligible and whether a particular unit was subject to a 340B discount. To ensure that pharmacies are provided the MFP discount in a timely manner, the TPA could potentially provide an initial discount payment to pharmacies within 14 days (following the TPA's initial screening for eligibility), with true-ups of the MFP discount if needed following verification by the manufacturer.

B. CMS Should Define the MFP Discount as the Difference between the MFP and ANFAMP

Exelixis disagrees with CMS's intention to use a dispensing entity's actual acquisition cost as the point of comparison for determining the MFP discount amount. The actual acquisition cost can be highly variable — both from pharmacy-to-pharmacy, as well as within a pharmacy if more than one wholesaler supplies a product to a pharmacy. We believe that it would be burdensome and operationally challenging to require pharmacies to report actual acquisition costs. For example, the variability in acquisition costs increases the risk that pharmacies may misreport their acquisition costs, which could lead to repeated corrections of the MFP discount amount. We instead propose that CMS define the MFP discount amount as the difference between the MFP and the ANFAMP of a selected drug. This is similar to how discounts are calculated for purposes of the TRICARE Retail Pharmacy (TRRx) Program, which provides the Department of Defense (DoD) the federal ceiling price (FCP) on drugs that are dispensed by community pharmacies and reimbursed by TRICARE. The TRRx rebate amount is calculated as the ANFAMP (which approximates the pharmacy acquisition price) less the FCP.¹⁰ Using ANFAMP, rather than actual acquisition cost, is also consistent with the structure of the IRA, given that the MFP ceiling is determined in part based on a selected drug's Non-FAMP.¹¹ Because the calculation of ANFAMP includes chargeback-based discounts that are processed through wholesalers to end customers, including pharmacies, it is also a better approximation of pharmacy acquisition costs than benchmark prices, such as Wholesale Acquisition Cost (WAC).

⁸ 42 C.F.R. § 423.2315(b)(3).

⁹ Interest Calculation for Late Rebate Payments, CMS, <https://www.medicaid.gov/medicaid/prescription-drugs/medicaid-drug-rebate-program/interest-calculation-for-late-rebate-payments/index.html#:~:text=In%20accordance%20with%20section%201927,before%20interest%20begins%20to%20accrue>.

¹⁰ 32 C.F.R. § 199.21(q)(3)(ii).

¹¹ SSA § 1194(c)(1)(A)-(C).

II. Consistent with the Statute, CMS Should Establish Mechanisms to Prevent MFP and 340B Duplicate Discounts

Under the IRA’s nonduplication provision, a manufacturer of a selected drug is not required to provide access to the MFP *and* the 340B ceiling price when a covered entity dispenses a selected drug to a Medicare beneficiary that is a “patient” of the covered entity.¹² Instead, manufacturers are required to provide access to *either* the MFP or the 340B price, whichever is lower.

Exelixis is concerned that despite the statutory nonduplication provision, there remains a significant risk of duplicate 340B and MFP discounts. For example, with respect to Medicaid and 340B duplicate discounts, the Office of Inspector General (OIG) has noted that even though such “duplicate discounts are prohibited by law . . . they . . . could occur in the Medicaid rebate process.”¹³ The Government Accountability Office (GAO) has expressed similar concerns, pointing to CMS’s “limited oversight of state Medicaid programs’ efforts to prevent duplicate discounts.”¹⁴ Therefore, we strongly encourage CMS to take seriously its statutory obligation to prevent duplicate MFP and 340B discounts and to establish robust safeguards.

At a minimum, we recommend that CMS require covered entities to identify units of selected drugs that are purchased under the 340B program when submitting a claim. It is widely-recognized that a 340B claims-level modifier requirement would help prevent duplicate discounts. OIG has recommended that CMS “require States to use claim-level methods to identify 340B claims,” noting that such requirement would “improve accuracy in identifying 340B claims and thereby reduce the risk of duplicate discounts.”¹⁵ Although CMS has declined to establish a universal claims level modifier requirement, a claims modifier is among the Agency’s recommended “best practices” for States to avoid 340B duplicate discounts in the Medicaid program.¹⁶ Exelixis is encouraged that for purposes of the Part D inflation rebate, CMS intends to require that a 340B indicator be included on the PDE record.¹⁷ Exelixis strongly encourages CMS to carry over this requirement to the Program. CMS also should require indicators for non-340B claims and reject claims without either indicator. This would reflect CMS’s approach for the discarded drug refund, where providers and suppliers submitting claims for single-dose container or single-use package drugs that are payable under Part B must include the “JW” modifier to note the amount of drug that was discarded, or, effective July 1, 2023, use

¹² SSA § 1193(d).

¹³ State Efforts to Exclude 340B Drugs from Managed Care Rebates, OIG (June 2016), <https://oig.hhs.gov/oei/reports/oei-05-14-00430.pdf>.

¹⁴ 340B Program: Oversight of Intersection with the Medicaid Drug Rebate Program Needs Improvement, GAO (Jan. 2020), <https://www.gao.gov/assets/gao-20-212.pdf>.

¹⁵ State Efforts to Exclude 340B Drugs from Managed Care Rebates, OIG (June 2016).

¹⁶ Best Practices for Avoiding 340B Duplicate Discounts in Medicaid (Jan. 2020), https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/cib010820_110.pdf.

¹⁷ Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1860D-14B of Social Security Act, and Solicitation of Comments, CMS (Feb. 9, 2023), *available at* <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>

the “JZ” modifier to attest that no amount of drug was discarded.¹⁸ CMS established the JZ modifier after “observ[ing] low compliance with JW modifier use.”¹⁹

CMS also should leverage the Program’s TPA (as described above) to help determine whether a claim for a selected drug is subject to a 340B discount, based on PDE data. The TPA could help facilitate the determination of whether an MFP discount or a 340B discount is owed, similar to the role of 340B TPAs or split-billing vendors with respect to Medicaid and 340B duplicate discounts. As stated above, after verifying that a claim is MFP-eligible, the TPA should provide certain claims-level data (including the 340B indicator) to a manufacturer so that the manufacturer can independently verify that the claim was not subject to a 340B discount and is eligible for the MFP.

In addition to the concerns described in Section I.A above, Exelixis has concerns that the 14-day timeframe for manufacturers to pay the MFP discount does not provide manufacturers with sufficient time to verify whether a claim also is subject to a 340B discount.²⁰ In recent years, pharmacies are increasingly using a “replenishment inventory model,” under which non-340B purchased drugs are initially dispensed to a patient and then “replenished” with 340B drugs once 340B patient eligibility is confirmed. In our experience, the lag between a pharmacy dispensing a drug and the 340B replenishment order often exceeds 14-days. Given OIG’s longstanding concerns that the replenishment model “creates complications in preventing duplicate discounts” in the Medicaid program,²¹ the Secretary should take steps to ensure that the replenishment model does not lead to duplicate discounts in the Medicare program as well. Specifically, the Secretary should impose a time limit after a unit of product is dispensed for a covered entity to determine whether the product is 340B eligible and replenish the unit at the 340B ceiling price. This time period must end before MFP invoices are compiled and sent to manufacturers. Then, manufacturers should have a reasonable period after the replenishment window has closed to verify whether a selected drug is subject to a 340B discount before providing the MFP discount. This would be consistent with other government discount and rebate programs, which under certain circumstances, permit manufacturers to verify and dispute whether a discount is required. Under the Coverage Gap Discount Program, for example, manufacturers have 60 days to dispute discounts on quarterly invoices.²² Under the Medicaid Drug Rebate Program, manufacturers also can dispute claims that were previously paid using the Prior Quarter Adjustment Statement (PQAS) process.²³

¹⁸ Medicare Program, Discarded Drugs and Biologicals — JW Modifier and JZ Modifier Policy, Frequently Asked Questions, <https://www.cms.gov/medicare/medicare-fee-for-service-payment/hospitaloutpatientpps/downloads/jw-modifier-faqs.pdf>.

¹⁹ *Id.*

²⁰ Initial Guidance § 40.4.

²¹ Memorandum Report: Contract Pharmacy Arrangements in the 340B Program, OIG (Feb. 4, 2014).

²² 42 C.F.R. § 423.2330(c)(1).

²³ CMS, Medicaid Drug Rebate Program Dispute Resolution, <https://www.medicaid.gov/medicaid/prescription-drugs/medicaid-drug-rebate-program/medicaid-drug-rebate-program-dispute-resolution/index.html> (last updated Mar. 2, 2023).

Exelixis believes that the safeguards that we propose above should be viewed as the baseline for reducing the risk of duplicate MFP and 340B discounts. We are concerned, however, that even with our proposed safeguards, it is not possible to eliminate duplicate discounts under the current structure of the 340B program. Currently, with the exception of certain AIDS Drug Assistance Program (ADAP) covered entities, manufacturers are required to provide upfront 340B discounts to all other covered entity types. This means that manufacturers currently do not have the opportunity to verify whether a patient qualifies for a 340B discount before providing the discount, which significantly increases the risk of diversion and duplicate Medicaid rebates, despite the respective statutory prohibitions.²⁴

The new MFP discount—coupled with the MFP/340B nonduplication provision and the replenishment model—introduce unprecedented complexity to the 340B program. Consistent with our support for retrospective MFP discounts (discussed in Section I.A.), we believe that the most effective way for the Agency to comply with the IRA’s nonduplication provision is if the Secretary also permits manufacturers to provide 340B discounts as a retrospective rebate to *all* covered entity types. Shifting to a 340B retrospective rebate is within the Secretary’s discretion, because the 340B statute permits the Secretary to implement the 340B program through a “rebate or discount, as provided by the Secretary.”²⁵ Permitting manufacturers to verify an individual’s eligibility for a 340B (or MFP) discount before such a discount is owed will promote program integrity and ensure compliance with statutory duplicate discount prohibitions.

III. CMS Should Implement the Small Biotech Carveout Consistent with Congressional Intent

Exelixis is disappointed that CMS is not soliciting comments on Section 30, which addresses foundational issues such as the exception for small biotech drugs (the “small biotech carveout”) and the definition of a qualifying single source drug. Doing so deprives stakeholders of a valuable opportunity to provide input on the Program to help support its implementation consistent with congressional intent. In particular, we note that the Initial Guidance does not provide *any* guidance on important aspects of the small biotech carveout, including the exception for new formulations. Despite a record of clear Congressional intent to preserve the ability of small biotechnology companies to continue their development of innovative medicines, Exelixis is concerned that the absence of definitive guidance from CMS on the scope of the small biotech carveout creates uncertainty as to whether that provision will safeguard the innovation of companies, like Exelixis, that it was intended to assist. Therefore, since the new formulations exception is not addressed at all in Section 30 of the Initial Guidance (and thus there is no guidance on this point for CMS to issue as final), we are submitting comments regarding the new formulations exception for CMS’ consideration in developing its revised Program guidance.

²⁴ Public Health Service Act § 340B(a)(5).

²⁵ Public Health Service Act § 340B(a)(1).

As described further below, Exelixis urges CMS to make clear that pursuant to the definition of qualifying single source drug set forth in the Initial Guidance—under which all dosage forms, strengths, and formulations that share the same active moiety and the same NDA holder are considered together—a qualifying single source drug must qualify as a small biotech drug for *all* of its formulations, provided the NDA holder retains ownership of these formulations (and thus they continue to constitute the same qualifying single source drug). We believe a contrary approach would be inconsistent with the statutory obligation to calculate a single MFP for each qualifying single source drug, and inconsistent with Congress’ intent to protect R&D incentives for small biotechnology companies.

A. Congress Intended to Protect R&D Incentives for Small Biotechnology Companies

A key principle underlying the IRA is to protect incentives for small biotechnology companies. In the lead-up to the IRA’s predecessor, the Build Back Better Act, Senate Finance Committee Chair Ron Wyden released a set of “Principles for Drug Pricing Reform.”²⁶ The principles set forth a mission: to “mak[e] prescription drug prices more affordable while encouraging innovation and scientific breakthroughs.”²⁷ Significantly, the principles recognized the unique and critical role of small biotechnology companies, stating that “[t]he research that led to these medical advances can largely be traced back to small biotechnology companies that take on a disproportionate share of the risk of R&D.”²⁸ Therefore, Chair Wyden indicated that drug pricing reforms should be “tailored to the scale of these companies, as well as other factors that affect their access to capital.”²⁹

All of the subsequent drafts of the drug pricing reform legislation—including the IRA, as enacted—reflect Chair Wyden’s commitment to protect small biotechnology companies. For example, one of the key provisions that Congress included in the IRA to protect small biotech manufacturers is the small biotech carveout. This carveout excludes “small biotech drugs” from the Program for three years, after which such drugs will have a temporary floor on the MFP determined under the Program.³⁰ Additionally, under the Part D redesign provisions of the IRA, certain smaller manufacturers (known as “specified manufacturers” and “specified small manufacturers”) will have their manufacturer discounts phased-in over a five-to-seven-year period.³¹

B. CMS Should Interpret the New Formulations Exclusion from the Small Biotech Carveout Consistent with the Statute and Congressional Intent

²⁶ Chairman Ron Wyden, Principles for Drug Pricing Reform 1 (June 2021), *available at* <https://www.finance.senate.gov/imo/media/doc/062221%20SFC%20Drug%20Pricing%20Principles.pdf>.

²⁷ *Id.* at 1.

²⁸ *Id.* at 3 (emphasis added).

²⁹ *Id.*

³⁰ SSA §§ 1192(d)(2)(A); 1194(d).

³¹ SSA § 1860D-14C(g)(4)(B)-(C).

Under the small biotech carveout, a “small biotech drug” is defined as “a qualifying single source drug” that satisfies certain Medicare expenditure thresholds.³² The IRA further states that “a new formulation, such as an extended release formulation, of a qualifying single source drug shall not be considered a [small biotech drug].”³³ CMS is not soliciting comment on section 30 of the Initial Guidance, which addresses the small biotech carveout and other foundational issues related to selection under the Program. We are deeply concerned that CMS’ decision to skip over the step of providing stakeholders an opportunity to comment before issuing final guidance deprives stakeholders of an important process protection and creates avoidable programmatic risk. Neither the Initial Guidance nor the separate Information Collection Request on the small biotech carveout³⁴ addresses the new formulation exclusion to the small biotech carveout at all, leaving manufacturers without a clear understanding of how CMS will determine whether their drugs qualify as small biotech drugs. Nevertheless, if CMS maintains the definition of qualifying single source drug set forth in the Initial Guidance, we believe that the statute requires a qualifying single source drug to qualify as a small biotech drug for *all* of its formulations, provided the NDA holder retains ownership of these formulations. In addition to securing other intended effects, this outcome will also protect the R&D incentives that drive investment in innovation like that demonstrated by Exelixis in its development of COMETRIQ[®] and CABOMETYX[®].

1. The MFP, and thus the Small Biotech Carveout, Applies Equally to All Formulations of the Same Qualifying Single Source Drug

Under the statute, the scope of a “qualifying single source drug” is significant at every stage of the Program. A qualifying single source drug that meets certain criteria is a negotiation-eligible drug,³⁵ and a negotiation-eligible drug that meets certain criteria is a selected drug.³⁶ CMS is required to establish a single MFP for each selected drug, as well as to “establish[] . . . procedures to compute and apply [that] maximum fair price across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug.”³⁷ Therefore, the statute establishes a chain under which a single MFP ultimately is determined for each qualifying single source drug that is selected under the Program.

The Initial Guidance defines a “qualifying single source drug” to include all dosage forms, strengths, and formulations of a product that share the same active moiety and the same NDA holder.³⁸ Because a single MFP will apply across all of these formulations, if CMS maintains the definition of qualifying single source drug set forth in the Initial Guidance,

³² SSA § 1192(d)(2)(A).

³³ SSA § 1192(d)(2)(C).

³⁴ 88 Fed. Reg. 4184 (January 24, 2023).

³⁵ SSA § 1192(d)(1).

³⁶ SSA § 1192(b).

³⁷ SSA § 1196(a)(1)-(2).

³⁸ Initial Guidance at 8.

Exelixis believes a qualifying single source drug must qualify as a small biotech drug for *all* of its formulations, provided the manufacturer retains ownership of the NDA of all of these formulations (and thus all formulations continue to constitute the same qualifying single source drug) and the qualifying single source drug meets the Medicare expenditure thresholds set forth in SSA § 1192(d)(2)(A).

2. Applying the Small Biotech Carveout to all Formulations of the Same Qualifying Single Source Drug Furthers the Innovation Incentives Underlying this Provision

As Congress recognized when enacting the IRA, small and mid-size biotechs, like Exelixis, play an increasingly larger role in discovering innovative medicines. This involves overwhelming challenges and inherent risks of failure at each step of the discovery, development, regulatory, and commercialization process. For example, during most of Exelixis' nearly 30-year history, the company operated without product revenue, taking significant risks to sustain formidable research facilities and clinical trials. Exelixis was founded in 1994, focused initially on early-stage scientific research before shifting exclusively to cancer. We used an industry-leading high throughput drug discovery process to identify compounds with therapeutic potential and advance them through preclinical and clinical development. As is typical, a large majority of these drug candidates failed. But, some succeeded, of which the most promising was cabozantinib. FDA approved COMETRIQ[®] (cabozantinib) capsules in 2012 to treat a small population of patients with a rare thyroid cancer.³⁹ We suffered a catastrophic event in late 2014 after two phase 3 registrational cabozantinib clinical trials failed in prostate cancer. These events forced us to restrict spending immediately, reduce our workforce by more than 70 percent, and focus our limited financial resources on two important and difficult-to-treat indications – kidney and liver cancer. Fortunately for seriously ill cancer patients and the company, cabozantinib demonstrated positive results in two large global pivotal trials, and CABOMETYX[®] (cabozantinib) tablets was approved in 2016.⁴⁰

CABOMETYX[®] is Exelixis' primary commercial product, and it is the culmination of decades of high-risk investments in cutting-edge science. We estimate that Exelixis invested over \$2 billion on the *separate* development of CABOMETYX[®], including internal and external work required to perform discrete clinical trials on each drug and efforts to achieve regulatory approvals. The significant time and expense to conduct additional clinical trials to obtain a new NDA for important and difficult-to-treat cancer indications is the sort of investment that Congress sought to protect and encourage through the small biotech carveout.

If CMS were to interpret the small biotech carveout to apply only to certain formulations of a qualifying single source drug — in spite of the statutory language to the contrary — CMS

³⁹ Drugs@FDA: FDA-Approved Drugs, New Drug Application (NDA): 203756, *available at* <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=203756>.

⁴⁰ Drugs@FDA: FDA-Approved Drugs, New Drug Application (NDA): 208692, *available at* <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=208692>.

would also be undermining Congress' intent to protect small biotech R&D incentives. Such an outcome would impose a heavy and irrational penalty on manufacturers that invest in improvements to the formulation of their existing products while also seeking new indications to benefit different patient populations, rather than just seeking FDA approval for new indications using the same, and perhaps less advantageous, formulation.⁴¹ Such a result would undermine innovation and frustrate the express goals of Congress in enacting specific protections for small biotech drugs. If CMS nevertheless intends to move forward with this interpretation, we believe it is imperative that CMS issue guidance and provide an opportunity for stakeholders to submit comments before finalizing its interpretation.

IV. Conclusion

Over the company's 29-year history, Exelixis' employees and investors have become accustomed to the natural turbulence of the biotechnology industry. We have also come to appreciate the tremendous influence that government incentives (and disincentives) can have upon biotech investment decisions, and how those decisions ultimately enhance or impede innovation. Although the IRA will fundamentally alter the future of biopharmaceutical innovation, we are encouraged that Congress recognized and expressed a desire to preserve innovation incentives, particularly for smaller biotechnology companies like Exelixis. It is therefore critically important that CMS implement the IRA consistent with the plain language of the statute and congressional intent.

For instance, the definition of an "MFP-eligible individual" and the MFP/340B nonduplication clause demonstrate Congress' intent to limit when manufacturers are required to provide access to MFP and 340B discounts. As a matter of program integrity, CMS must take seriously its statutory obligation to implement these key provisions. For example, CMS should establish robust safeguards to ensure that manufacturers are required to pay MFP discounts only after an independent TPA and the manufacturer verify that the patient is eligible for the discount. Additionally, given the unprecedented complexity that the MFP introduces to the 340B program, we urge the Agency to establish parallel safeguards and/or consider permitting manufacturers to provide retrospective 340B discounts. Such measures will help ensure that MFP discounts are provided only where Congress intended.

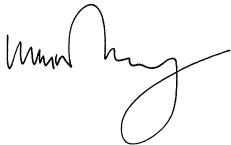
CMS also should carefully consider the impact of its policies on smaller biotechs, like Exelixis, that drive a significant share of medical innovation. We urge the Agency to clarify that a qualifying single source drug will qualify as a small biotech drug for *all* of its formulations,

⁴¹ Such a result would be an unprecedented disincentive to develop superior formulations and operate quite differently, for example, than the new formulations provision of the Medicaid rebate statute. Prior to the Affordable Care Act amendments to the Medicaid rebate statute, manufacturers could potentially reduce their Medicaid rebate liability by launching new formulations of certain covered outpatient drugs. The Affordable Care Act amendments removed this incentive for launching a new formulation, but they did not *penalize* manufacturers for launching new formulations. Affordable Care Act § 2501(d) (as amended by Health Care and Education Reconciliation Act of 2010 § 1206(a)) (codified at SSA § 1927(c)(2)(C)).

provided the NDA holder retains ownership of these formulations. Such an outcome is mandated by the statute and consistent with Congress' intent to maintain incentives for innovation, particularly by small biotechnology companies. It is an important step to help achieve Congress' intention of encouraging such businesses to invest further in the next generation of lifesaving treatments.

We hope CMS will take these comments into consideration when developing revised Program guidance. We would be happy to answer any questions that CMS may have regarding the topics we address herein.

Sincerely,

A handwritten signature in black ink, appearing to read 'Michael M. Morrissey', with a stylized, flowing script.

Michael M. Morrissey, Ph.D.
President and Chief Executive Officer
Exelixis, Inc.



EYEPOINT

PHARMACEUTICALS

April 13, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRARebateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

EyePoint Pharmaceuticals, Inc. ("EyePoint") appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance). EyePoint is a company committed to developing and commercializing therapeutics to help improve the lives of patients with serious eye disorders.

Although the agency isn't specifically requesting feedback on Section 30 of the Drug Price Negotiation Program at this time, we believe it is important for the agency to understand that Section 30, as currently drafted, could have a significant, detrimental impact on EyePoint's ability to develop and commercialize innovative therapeutics for patients. The current language in the draft for Section 30 allows for only 9 years between the granting of an NDA and setting of a Maximum Fair Price for small molecule therapies versus 13 years for biologic, large molecule therapies. This will put companies such as EyePoint, which develops small molecule extended delivery therapeutics that help prevent blindness and are injected into the retina and that compete with multiple biologic therapies, at a serious disadvantage, which may ultimately impact patient care. Companies such as ours may be forced to hold on making FDA submissions for NDAs until all of the potential indications have been studied rather than try to get the product to market for individual indications in a more expedient manner. This will obviously negatively impact patient care as patients in need would be denied an opportunity for a newly approved therapy for a longer period of time.

Secondly, as EyePoint and other similar companies intend to continue developing new and innovative small molecule therapies, Section 30, as presently drafted, will inevitably require us to emphasize and prioritize development programs that are more likely to generate a more rapid positive return in order to compete with new biologic treatments, and will diminish our willingness and ability to take on risks associated with the development of small molecule therapies that are less likely to achieve commercial success within the 9-year time frame of Section 30.

We appreciate your consideration of our comments as you develop the Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to patients from the reduced or delayed availability of innovative medicines is minimized.

Sincerely,

Nancy Lurker
CEO, EyePoint Pharmaceuticals, Inc.

April 14, 2023

Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Submitted via email to Centers of Medicare and Medicaid Services

RE: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure,

Families USA (FUSA) is a leading national, non-partisan voice for health care consumers, dedicated to the achievement of high quality, affordable health care and improved health for all. Central to realizing that vision is reducing the burden of prescription drug costs on America's families.

The high and rising cost of prescription drugs in the United States is a profound health problem and a significant economic burden on our nation's families, including people who rely on Medicare for their health coverage. Large drug corporations, in their efforts to maximize profits, too often raise the prices of both existing and new prescription drugs to obscene, price gouging levels. As a result, U.S. drug prices are nearly twice as high as prices in other comparable countries, even after rebates.ⁱ And millions of Medicare beneficiaries, particularly lower-income and Black and Latino beneficiaries, struggle to afford the prescription medications that they need due to cost.ⁱⁱ

FUSA applauds the Biden Administration and the Centers for Medicare and Medicaid Services (CMS) for taking the first major step in implementing the historic reform of prescription drug pricing in the Medicare program, issuing proposed program guidance for the negotiation process for selected drugs whose negotiated prices would be available beginning in 2026 (i.e., Initial Price Applicability Year 2026). We appreciate the opportunity to comment on this proposed guidance and appreciate all of the work from CMS to facilitate lower drug costs for millions of older adults and people with disabilities. There are aspects of the guidance that we support but chose not to reflect on in this comment in order to prioritize a few key areas of recommendations.

We believe it is critical for the experiences of the millions of people who rely on Medicare to access affordable prescription drugs to remain the focus of implementation efforts. To that end, this comment letter will provide recommendations across the following areas:

1. Soliciting Public Comments Regarding the Implementation of the Medicare Drug Negotiation Program
2. Section 60.3: Methodology for Developing an Initial Offer
3. Section 40.2.1: Confidentiality of Proprietary Information & Section 60.6: Publication of the MFP

4. Section 40.4: Providing Access to the MFP
5. Section 60.3.4: Consideration of Manufacturer-Specific Data & Section 100.2: Violations of the Agreement
6. Section 50.2: Evidence About Therapeutic Alternatives for the Selected Drug

1. Soliciting Public Comments Regarding the Implementation of the Medicare Drug Negotiation Program

Under the Administrative Procedures Act (APA), CMS is required to provide an opportunity for public comment on any proposed rules or regulations as they relate to any new or existing law. However, in the case of the IRA's drug price negotiation provisions, the IRA waived these requirements and directs CMS to implement many of the law's drug negotiation provisions through sub-regulatory "program instruction or other forms of program guidance" for the parts of the process that lead to maximum fair prices that take effect beginning in 2026, 2027, and 2028. Despite the IRA's waiving of APA requirements, CMS has indicated it will voluntarily solicit comments on a number of areas in its Medicare Drug Negotiation Proposed Guidance.

FUSA applauds CMS for voluntarily providing the public opportunities to submit feedback regarding implementation of the Medicare Negotiation Program, including soliciting comments for the majority of its draft guidance on the Medicare Drug Negotiation Program, as it relates to "Initial Price Applicability Year 2026." This is a critical step to ensuring that the needs of families and consumers are prioritized as CMS implements the Medicare Drug Negotiation Program, allowing the public, including consumer and patient advocates, sufficient opportunities to provide input to inform negotiation policy decisions.

2. Section 60.3: Methodology for Developing an Initial Offer

The IRA requires CMS to develop and apply a consistent methodology and process for negotiating with drug manufacturers to arrive at a maximum fair price. It clearly states that CMS must develop a negotiation process that "aims to achieve the lowest maximum fair price for each selected drug."

A vital step in the negotiation process is how CMS arrives at the initial price that it offers to drug manufacturers. The law lists nine factors that CMS is required to "consider" when calculating an initial and final maximum fair price offer. However, the IRA provides no direction for how CMS should prioritize, weight, or define these factors when arriving at a pricing decision.

In the proposed guidance, CMS outlines its plan to calculate an initial maximum fair price offer to drug manufacturers based on a three-step process. First, CMS will identify therapeutic alternatives for the selected drug subject to negotiation and calculate the Part D net price(s) of those therapeutic alternatives.^{iii,iv} Second, based on the prices of those therapeutic alternatives, CMS will begin developing an initial price offer, and adjust that offer "relative to whether the selected drug offers more, less, or similar clinical benefit compared to its therapeutic alternatives," to arrive at a "preliminary price." Third, CMS will adjust the preliminary price based on a number of manufacturer-specific data. For example, CMS would lower the price depending on whether federal support was received for drug discovery and development or whether the selected drug has patents or exclusivities that last for a number of years.

We are appreciative of CMS' efforts in proposing a process for developing an initial price offer with limited statutory direction. We are also supportive of CMS' intent to adjust the maximum fair price offer based on comparative effectiveness research, such as patient-reported outcomes and patient experience data as well as manufacturer specific data (e.g., research and development costs, unit costs of production). **However, we are deeply concerned with CMS' proposed approach to anchoring the initial "preliminary price" based off Part D net prices of therapeutic alternatives.** There is substantial evidence that the drug prices paid by Medicare Part D are significantly inflated compared to the prices paid by other public payers within the United States, as well as prices paid by other comparable countries.^{v,vi,vii} For instance, according to the Government Accountability Office, Part D net prices were at least two to four times higher than publicly available prices in comparable countries in 2020.^{viii} We are concerned that Part D net prices do not reflect the true value of these medications and relying on them as a fundamental starting point for Medicare drug negotiation would undermine the Medicare Drug Negotiation Program and the program's ability to achieve meaningful cost savings for consumers and families. CMS acknowledges these concerns in their own proposed guidance, stating that the Part D net prices associated with the "therapeutic alternative(s) for a selected drug may not be priced to reflect its clinical benefit...."^{ix}

Based on the concerns above, **FUSA strongly encourages CMS to reassess its approach to developing a maximum fair price offer, avoiding the use of Part D net prices as a starting point.**

Instead, we encourage CMS to employ a cost-effectiveness approach to develop a preliminary price range, which could then be adjusted to arrive at a maximum fair price. Specifically, we recommend CMS establish non-biased (see discussion below at comment # 6) cost-effectiveness targets or thresholds that serve as an initial price range for each selected drug, and which could then be adjusted based on comparative effectiveness research, the prices of therapeutic alternatives, and other manufacturer specific data to arrive at a maximum fair price. To calculate these targets, CMS should, in consultation with the HHS Office of the Assistant Secretary for Planning and Evaluation, determine an upper and lower bound cost or price per unit of health gained (as well as cost per condition-specific measure of clinical benefit) that it deems appropriate and reflective of the opportunity cost of the treatment in relation to the treatment's added net benefits for Medicare patients over time.^x

We believe the cost effectiveness approach outlined above guarantees that the maximum fair price calculated by CMS truly reflects the therapeutic value of the drug subject to negotiation and, importantly, avoids relying on prices, such as Part D net prices, that are all too often the result of widespread market failures and pharmaceutical industry gaming.^{xi} Further, this approach has the added benefit of providing the strongest financial incentives for drug manufacturers to focus on true therapeutic innovations.

3. Section 40.2.1: Confidentiality of Proprietary Information & Section 60.6: Publication of the MFP

The public reporting requirement of the final maximum fair prices and an explanation for how it arrived at each maximum fair price, including which factors were considered is important because it provides the public and other payers of prescription drugs with access to information on the value of select high-priced prescription drugs and what a fair price may be. This information is critical for the public and people who rely on Medicare for their health coverage to understand CMS' justification for arriving at a final maximum fair price for a selected drug, and to increase transparency around the underlying cost and value for the prescription drugs subject to negotiation. Additionally, this level of transparency is essential for other payers to be able to effectively negotiate the prices of prescription drugs with drug

manufacturers and exert downward pressure on the price of prescription drug price across the entire U.S. market. Notably, the IRA affords CMS wide discretion to decide which information used to calculate a maximum fair price is made public or is “proprietary” and not made public.

FUSA is disappointed with CMS’ proposal to treat the vast majority of the manufacturer specific data it would receive as proprietary and therefore would not be public. CMS intends to keep the following information non-public, unless already made public through other means, such as: non-Federal average manufacturer price, research and development costs and recoupment, unit costs of production and distribution, pending patent applications, and market data and revenue and sales volume data.

FUSA is also disappointed with CMS’ proposal to only provide “high level comments” when disclosing a public justification for how it arrived at a maximum fair price(s) during negotiation. CMS intends to only include high level comments explaining the maximum fair price without sharing any information that it deems as proprietary, such as research and development costs.

There is a strong public interest to ensuring the Medicare Drug Negotiation Program is achieving its statutory mandate of achieving the lowest maximum fair price possible. Without transparency into key data that CMS is using to inform a maximum fair price, the integrity of the Medicare Drug Negotiation Program is at heightened risk for industry gaming or sabotage. Further, making this data publicly available could help to spur competition in the private insurance market and help drive down prices for consumers and families who rely on private, employer sponsored insurance coverage. **FUSA strongly urges CMS to reconsider the extent to which it categorizes certain manufacturer specific data as proprietary and at a minimum make public the following information: non-Federal average manufacturer price, research and development costs and recoupment, and unit costs of production and distribution.**

Further, FUSA urges CMS to implement the IRA’s reporting requirement in a way that publicizes as much information as possible. This includes which factors and value frameworks were used to come to their decision regarding a maximum fair price, as well as any information received from drug manufacturers.

4. Section 40.4: Providing Access to the MFP

To ensure the IRA and the Medicare Drug Negotiation Program truly results in lower drug prices for people who rely on Medicare, it is critical that families and consumers have access to the lower negotiated price at the pharmacy counter and at point of sale. In its proposed guidance, CMS has indicated it plans to require that the “negotiated price of a Part D drug is the basis for determining beneficiary cost-sharing and for benefit administration at the point of sale.” **FUSA applauds CMS for taking this critical step to ensure every consumer and family that relies on Medicare for their health care needs has access to and benefits from the lower negotiated price for drugs that are selected for Medicare negotiation.**

FUSA also applauds CMS for planning to conduct ongoing oversight and monitoring to ensure that every eligible individual, including all Medicare beneficiaries, have access to the lower negotiated prices for selected drugs. Continuous monitoring and oversight of drug manufacturers and pharmacies is critical to ensuring no entity across the prescription drug supply chain, including drug manufacturers, wholesalers, pharmacy benefit managers, or pharmacies, are taking advantage or gaming the Medicare Drug Negotiation to their benefit and to the detriment of consumers and families.

5. Section 60.3.4: Consideration of Manufacturer-Specific Data & Section 100.2: Violations of the Agreement

As CMS begins the drug negotiation process, it will request information from drug manufactures to inform its calculation of maximum fair prices and as part of the negotiation process. According to CMS' proposed guidance, this will include requesting information from drug manufacturers on their research and development costs; current costs of production; data on pending and approved patent applications; market data; sales information; and non-Federal average manufacturer price.

While we applaud CMS for confirming that manufacturers would be subject to civil monetary penalties if manufacturers knowingly provide false information to CMS as part of the Medicare Drug Negotiation Program, **FUSA is deeply concerned that CMS is proposing to rely on the “assumptions and calculations” related to certain manufacturer specific data, such as research and development costs, that are reported to CMS by manufacturers with limited oversight or independent verification.** Drug manufacturers often game government reporting systems to their benefit. For example, it was found that many manufacturers have misclassified their drugs as generics, thus paying significantly less in rebates under the Medicaid Drug Rebate Program, resulting in more than a billion dollars in overcharges.^{xii}

FUSA strongly encourages CMS to develop additional guardrails in order to closely scrutinize any data reported by drug manufacturers on their drug sales and related prices. CMS should rely on independent data sources whenever possible and consider contracting with an audit firm or firms for any otherwise unaudited manufacturer data. It is essential that all of the information used to inform the Medicare negotiations are accurate and complete to ensure that CMS has the information it needs to calculate *truly* fair prices.

6. Section 50.2: Evidence About Therapeutic Alternatives for the Selected Drug

In their effort to consider alternate treatments for selected drugs, CMS is required to not use measures that would evaluate or weight the life of an elderly, disabled, or terminally ill person as any less than another life. This guidance bars CMS from using Quality Adjusted Life Years (QALYs) as a measurement tool. **There are many promising frameworks and methodologies to help assess health care value, and that importantly do not discriminate on the basis of disability, age, or any other protected status; we are supportive of restrictions for the use of QALYs and strongly encourage CMS to identify other measurement tools to assess therapeutic value.**

We want to specifically highlight usage of “Equal Value of Life Years Gained,” or EvLYG, which is a metric that measures gains in length of life of a given treatment in a way that ensures that all years of life are valued equally.^{xiii} EvLYG is an evaluation tool we support CMS using, as it allows for a treatment's value and quality to be assessed without disproportionately affecting certain populations.

Conclusion

Families USA greatly appreciates CMS for taking this important step to implementing the Medicare Drug Negotiation Program. Authorized by the IRA, this historic health care reform holds the promise of reducing the high cost of prescription drugs and helping ensure that consumers and families that rely on

Medicare for health coverage truly have access to affordable, live-saving medications. Families USA looks forward to continuing to work with CMS on the implementation of this program, as well as other efforts to lower the high cost of prescription drugs.

Thank you for your time in considering these comments. Please contact Aaron Plotke (APlotke@familiesusa.org) and Hazel Law (HLaw@familiesusa.org) with any questions.

Sincerely,



Frederick Isasi

Executive Director
Families USA

ⁱ Mulcahy AW, C.; Tebeka, M.; Schwam, D.; Edenfield, N.; Becerra-Ornelas, A. International Prescription Drug Price Comparisons. 2021;
https://www.rand.org/content/dam/rand/pubs/research_reports/RR2900/RR2956/RAND_RR2956.pdf. Accessed November 12, 2021.

ⁱⁱ Tarazi, W., Finegold, K., Sheingold, S., De Lew, N., and Sommers, BD. Prescription Drug Affordability among Medicare Beneficiaries (Issue Brief No. HP-2022-03). Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. January 2022

ⁱⁱⁱ According to CMS' proposed guidance, therapeutic alternatives will only include pharmacological treatments (as opposed to non-pharmacological treatments), and only treatments covered by Medicare Part D.

^{iv} If no therapeutic alternatives exist or the prices of the therapeutic alternatives exceed the statutory ceiling price, CMS proposes to base the initial starting point price based off the Federal Supply Schedule (FSS) or "Big Four Agency" price. If the FSS or "Big Four Agency" price exceeds the statutory ceiling price, then CMS proposes to use the statutory ceiling as the starting point for the initial price offer.

^v Government Accountability Office, *Prescription Drugs: Department of Veterans Affairs Paid About Half as Much as Medicare Part D for Selected Drugs in 2017*, GAO-21-111, January 14, 2021.

^{vi} Mulcahy AW, C.; Tebeka, M.; Schwam, D.; Edenfield, N.; Becerra-Ornelas, A. International Prescription Drug Price Comparisons. 2021;
https://www.rand.org/content/dam/rand/pubs/research_reports/RR2900/RR2956/RAND_RR2956.pdf. Accessed November 12, 2021.

^{vii} Government Accountability Office, *Prescription Drugs: U.S. Prices for Selected Brand Drugs Were Higher on Average than Prices in Australia, Canada, and France*, GAO-21-282, April 28, 2021.

^{viii} Ibid.

^{ix} See page 49, CMS, *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments*. March, 15, 2023.

^x This recommendation is based on the Institute for Clinical and Economic Review's *2020-2023 Value Assessment Framework*, January 31, 2020 (Updated February 3, 2022). For more information, see https://icer.org/wp-content/uploads/2020/11/ICER_2020_2023_VAF_02032022.pdf.

^{xi} Families USA, *Our Broken Drug Pricing and Patent System Diverts Resources Away from Innovation and into Mergers, Patent Gaming and Price Gouging*, August 2021. https://familiesusa.org/wp-content/uploads/2021/08/RX-2021-209_Innovation-Drug-Pricing-Issue-Brief.pdf

^{xii} Department of Health and Human Services, Office of Inspector General, *Potential Misclassifications Reported by Drug Manufacturers May Have Led to \$1 Billion in Lost Medicaid Rebates* (OEI-03-17-00100) (HHS OIG, December 2017), <https://oig.hhs.gov/oei/reports/oei-03-17-00100.pdf>

^{xiii} ICER, *The QALY: Rewarding the Care that Most Improves Patient's Lives*, December 2018.

The Honorable Meena Seshamani, M.D., Ph.D
Deputy Administrator and Director of the Center for Medicare
Department of Health & Human Services
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Dear Deputy Administrator Seshamani,

On behalf of First Databank (FDB), a trusted leader in drug knowledge for over 40 years, we appreciate the opportunity to comment on the Centers for Medicare & Medicaid Services' (CMS) initial guidance regarding Inflation Reduction Act requirements. CMS has issued guidance on establishing an inflation rebate for single source drugs and biological products, as well as establishing an MFP ceiling for designated drugs that covers both Medicare Part B and Part D. FDB is writing in response to the agency's request for comments on this guidance.

In order to make CMS's guidance on implementing an MFP ceiling effective and transparent, we urge the agency to publish the list of selected drug moieties, their respective NDCs, and unit-level MFPs in a structured and machine-readable format. Additional clarity surrounding data elements and definitions in the final publication, such as dosage forms and strength-specific MFPs would be paramount to making this implementation a success. A preliminary test file should be made available to all interested parties, along with the definition and layout of each data element. In addition, the schedule of release for the expected updates should be published in advance so that users of the content know when to expect the updates.

We acknowledge that CMS is intending to use the NDC-9 to derive unit-level MFPs to be applied across all strengths and dosage forms for negotiation. FDB recommends additional context be provided in terms of the final, negotiated unit-level MFPs and the format in which this report will be disseminated to the public as it relates to the FDA's proposed rule on the NDC-12 format. We hope CMS takes into account the structure and formatting of future file releases which will be impacted by the FDA's proposed rule.

We appreciate your consideration of these issues. Please contact me if you have any questions.

Thank you for your time.

Ethan Chan, PharmD, MS (he/him/his)
Senior Product Manager
FDB (First Databank, Inc)



VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
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Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Frontier Medicines appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

As the child of first-generation immigrants, I saw our pediatrician help my parents save my four-year old brother and then was devastated as we watched that heroic doctor swiftly perish from an incurable cancer. As a result, I decided at a young age to devote my life to science and finding new medicines that save lives. That is my American Dream. I co-founded Frontier Medicines to deliver drugs against undruggable targets – small molecule drugs that have the potential to be transformative for patients, including those with cancer that is currently untreatable.

Now, having been on both sides of the innovation equation, as both a biotech investor and founder of multiple biotech companies, I know the incredible amount of effort it takes to develop new medicines. I also know first-hand the benefits possible for patients when innovation is allowed to flourish, having

played a part in discovering first-in-class, precision medicines such as Ayvakit and Retevmo. These small molecule drugs have not only improved and prolonged the lives of patients with the rare disease and cancers they treat, but also helped people return to normal life. Today, the companies I've started employ nearly 1,000 Americans across the country—all working to give patients better options for tomorrow. With the IRA's arbitrarily short timeline for small molecule drugs, the U.S. government is actively discouraging future biotech innovation in this country – a sector America currently leads in the world. As currently written, the draft CMS guidance will hurt, not help, Medicare patients. The guidance penalizes small molecule medicines, medicines which currently are powerful tools in the efforts to treat deadly cancer and the toughest of diseases.

Furthermore, the current guidance actively discourages the innovation of medicines for rare and orphan diseases—essentially limiting efforts to only one disease area. In the wake of the IRA's passage, we are already seeing companies and those who fund them forced to step away from exploring additional rare disease medications and usage. One has to wonder how many Medicare patients and loved ones will go without new treatments in the future as a result.

In rushing to implement the IRA, the U.S. government is actively discouraging future biotech innovation in this country – a sector America currently leads in the world. Before we destroy one of the major American success stories, we need to take the time to get this right. Otherwise, patients will suffer in the years to come, as will the employees of small biotech companies who are trying to help them. Fixing the IRA matters to all of us. When innovation suffers, patients are the ones who lose.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact Victoria Fort, VP of Corporate Affairs at Frontier Medicines, by email at Victoria.fort@frontiermeds.com if you have any questions regarding our comments.

Best regards,

Chris Varma, Ph.D.

Co-founder, chairman, & CEO

Frontier Medicines Corporation

151 Oyster Point Blvd., 2nd Floor

South San Francisco, CA 94080

George C. Landrith
President & CEO



Senator Malcolm Wallop
(1933 - 2011)
Founder

April 14, 2024

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator
Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-1850

RE: Medicare Drug Price Negotiation Program Guidance

Dear Director Seshamani:

Frontiers of Freedom, founded in 1995 by U.S. Senator Malcolm Wallop, is an educational foundation whose mission is to promote the principles of individual freedom, peace through strength, limited government, free enterprise, free markets, and traditional American values.

I have served as the organization's President and CEO since 1998.

I appreciate the opportunity to provide comments to the Centers for Medicare & Medicaid Services' Initial Implementation Guidance and related Fact Sheet released March 15, 2023.

My primary focus will be Section 40.2.2, covering Data Use Provisions and Limitations of the Initial Implications Guidance. This section expressly prohibits pharmaceutical manufacturers from disclosing any information from CMS's initial offer, including the ceiling price. This section further prohibits the audio or visual recordings of such discussions, nor other dissemination of content written or verbally discussed during the negotiation period.

Additionally, CMS proposes that manufacturers destroy all correspondence and other information shared concerning any drug or biologic no longer qualifying as a selected drug. This includes all information received during the negotiation or renegotiation periods.

I believe these provisions violate core principles of American values and will undermine the goals that the negotiation process was established to achieve. My response will address three key problems inherent to this section of the drug price negotiation process:

1. Limitation of the proposed rules on manufacturers' Freedom of Speech
2. Hindrance of transparency and deterioration of stakeholder confidence
3. Limitations on good-governance standards and industry-level shared learning

Limitations of the proposed rules on manufacturers' Freedom of Speech

The notion of barring private sector participants from discussing aspects of "negotiating" with government regulators is antithetical to the basic tenets of free speech. This statutory gag order constitutes a clear governmental restraint on speech. The U.S. Supreme Court has long held that restraints on speech constitute a "most serious and the least tolerable infringement on First Amendment rights."

Manufacturers should be free to express their views on government activities relating to the price negotiation program as well as any other matter. Access to pharmaceuticals is critical for millions of Americans – and open discussion as to how drug prices are set is of paramount importance ensuring access to and development of medicines.

Hindrance of transparency and deterioration of stakeholder confidence

The proposed limitations on the free speech of bidding-process participants will erode public confidence in the price-setting process. By design, patients and other stakeholders may not know for months, if ever, important disclosures relating to drug price negotiations. Those relying on these treatments will naturally question why the process is shielded from scrutiny.

Such suspicion is expected given the proposed lengths CMS intends to go to in avoiding disclosure. CMS' proposed requirement that a "Certificate of Data Destruction" must be submitted within 30 days of a drug or biologic no longer qualifying as a selected drug will raise serious public concerns about what is happening behind the scenes.

Transparency should be present throughout the negotiation and renegotiation period(s) without explicit requirements to destroy all notes, emails, or other communiques relating to the initial offer and any subsequent offers. At the Federal level, such actions would be at odds with basic government FOIA and record retention principles, which are key elements of any good-governance approach. Yet under these rules, manufacturers are required to hide and destroy materially valuable information.

Limitations on good-governance standards and industry-level shared learning

This loss of transparency also muzzles manufacturers from pointing out flaws, oversights, or methodological problems in CMS' administration. Given the scale of the new price

FRONTIERS *of* FREEDOM

negotiation program, such feedback is critical to iteratively improving how bidding is conducted as well as its compliance monitoring.

The proposed gag order will also prevent future program participants – i.e., the inventors of tomorrow's life-saving medicines – from learning from previous bidding processes. This hurts small life-science firms, steepens the learning curve, and creates a distinct competitive advantage to existing manufacturers.

Encouraging Transparency

The research companies that research, develop, manufacture, and sell life-extending and life-saving drugs to the nation's 65 million Medicare participants are a critical part of the healthcare ecosystem. Manufacturers' ability to freely and openly share information on the drug-price negotiation program will be critical to the public's confidence in Medicare. Transparency and data sharing should be encouraged, not prohibited.

Sincerely,

A handwritten signature in blue ink that reads "George Landrith". The signature is fluid and cursive, with the first name "George" and last name "Landrith" clearly distinguishable.

George Landrith
President
Frontiers of Freedom



UNIVERSITY *of* WASHINGTON

SCHOOL OF PHARMACY

The Comparative Health Outcomes, Policy, & Economics (CHOICE) Institute

April 14, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
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200 Independence Avenue, SW
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IRARebateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

We are submitting this letter as independent health economists with a long history of collaboration on pharmaceutical policy analysis. In the interests of transparency, we declare that much of this work has been funded by pharmaceutical companies. We appreciate the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

We would like to comment in particular on Section 1193(e)(1) on “Manufacturer-specific data.” This section requests information on a number of items related to research and development (R&D) costs, production and distribution costs, recoupment, and related revenue items. We believe this request reflects a fundamental misunderstanding of the economics of the regulated U.S. and global pharmaceutical marketplace. Even if compliance with this request for R&D costs were possible (which is highly questionable), the submitted estimates would be irrelevant to the determination of the Maximum Fair Price (MFP) for a specific product. This is not to say that evidence and value do not matter. Indeed, in determining MFP through negotiation, the statute does specify what we see as the critical factor: “(A) The extent to which such drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives.”

The current market for innovative medicines is regulated through a combination of intellectual property protection (patents and exclusivities) and regulatory (Food & Drug Administration; FDA) statutes and regulations. The result is what economists call a “market design” that

incentivizes medical innovation by offering potentially high (but uncertain) rewards for high-risk investments, but then uses competition to keep down prices at later stages of the product life cycle. Patent-protected FDA-approved products that offer additional patient benefit have some degree of monopoly power through the period of protection that results from these patent and regulatory exclusivity provisions. For most new drugs, the protection averages 12 to 16 years (Kesselheim et al., 2017). During this period, the manufacturer has the exclusive right to market their compound: copies are not allowed to be marketed. This does not mean, however, that they do not face competition in the same drug class: other compounds with the same biological target and mechanism of action can compete with them. The market design is “oligopolistic competition” among single-source products. The best product in the class may receive a premium price and substantial rewards during this period of protection. But, by law, eventually the effective market exclusivity period will end and either generic or biosimilar versions (in the case of biologics) will be allowed to compete with the originator and others in the drug class. The value of this monopoly power is thus limited by market competition and by time. It is well known that about nine in 10 products fail during development: there is no guarantee that their costs are recouped in any way. Rather, the market design is that the rewards to the investors in the successful product will have to cover the costs of failures to sustain the market. The rewards to any one product, in fact, should be viewed against the cost of the 10 products needed to yield that one success. Thus, the product-specific R&D costs of any one product are irrelevant to the rewards it does (or does not) earn in the marketplace.

Indeed, imagine that an innovator discovered the cure for Alzheimer's disease based on a brilliant insight into molecular biology with a mechanism of action that was so compelling that it gained approval based on a small, low-cost trial using a surrogate marker that everyone accepted. Would we say that that innovator should only receive a small reward for such a miracle cure because its product-specific development costs were low? Some might argue that, but that ignores how the incentives in this investment system have operated for over 50 years. Of course, as we know, many billions of dollars have been spent by the industry on Alzheimer's disease research and thus far very little of this investment has been recouped. This lack of success is, of course, a concern for patients and their families, but it shows the market design is working. Money is going into R&D for diseases that matter, even where the science is difficult, i.e., where companies see high returns if they can deliver treatments that provide additional health benefit to patients.

The Inflation Reduction Act (IRA) does not directly or explicitly propose to move from this high-risk/high-reward market design to an alternative market design that is an essentially “cost-plus” marketplace with a regulated rate of return. But this may be the consequence of the proposed negotiation process for a MFP. While there can be an argument for such a cost-plus regulation in some markets where monopoly power exists — such as parts of the utility sector — it makes little sense in the complex life sciences industry with many competitors: many of whom will fail due to the complexity of the science, and with government granting of temporary market power only for successful products. We assume that CMS is not seeking to change the fundamental life sciences R&D market design which is based on incentives to reward medical advances with such temporary market power. In which case, these historical R&D costs are irrelevant to the value that patients and payers place on any specific product.

Furthermore, from a cost-accounting perspective, given that the rollout of this program will be for products that have been on the market for at least seven years, we surmise that, as most companies cannot accurately answer these questions for products they are about to submit to the FDA, they certainly will not be able to answer them for past products. They have not done the historical cost-accounting on a product-specific basis that would allow such tracing and linkage to individual products. Although estimates of the cost of specific trials could, in principle, be produced, the costs of all the individuals in the biopharmaceutical organization who are working on multiple products during the pre-launch (including discovery and pre-clinical) period are not routinely tracked or allocated to a specific product. Thus, it would most likely be infeasible to provide this information accurately. Of course, assumptions and estimates could be made, but to what end? They are irrelevant to the value of any specific product to Medicare beneficiaries, and they would not in any case adequately address the cost of failures.

In order to explore the challenges of estimating R&D costs, consider the estimates of drug development costs that have appeared in the literature. As the 2021 Congressional Budget Office report (CBO, 2021) makes clear, success rates vary by therapy area, reflecting the diverse scientific challenges, but also making an attribution of relevant failure costs even more difficult. Identification and attribution of discovery and pre-clinical costs is also challenging. The duration of the R&D process is important, as it affects the cost-of-capital component of any estimate of “successful” R&D expenditure. Of the three studies discussed by the CBO:

- Prasad and Mailankody (2017) dealt with earlier research (i.e., discovery and pre-clinical) expenditures and with the large number of failures by including all R&D costs for their (single product) companies. However, this has a survivor bias, in that the R&D costs of companies working in the same areas that go out of business are not included.
- Wouters et al. (2020) used Securities and Exchange Commission (SEC) filings to estimate discovery and pre-clinical expenditures and the analysis by Wong et al. (2019) of success rates by clinical area to multiply up estimates to take account of failures: i.e., they attempted to estimate the “system-wide” costs associated with bringing an individual product to market. As Cutler (2020) points out, Wouters et al. recognize that they are likely to have underestimated pre-clinical costs because of the difficulty of linking them to a specific molecule.
- DiMasi et al. (2016) used aggregate company R&D expenditures to estimate discovery and pre-clinical expenditures along with success/failure rates taken from a broader industry wide database of clinical success rates by stage. Again, this is an attempt to estimate costs including non-product specific discovery and pre-clinical costs and take account of failures that are not specific to the company concerned. The authors also sought to identify post-launch R&D costs, recognising that evidence of comparative effectiveness is increasingly collected post-launch.

In summary, the literature indicates the challenges of estimating R&D costs attributable to one product, and the difficulty of taking account of failures at the level of one company.

Questions about the current costs of the manufacturing and distribution of a product near the end of its exclusivity could conceivably be answered. Companies do have some idea of what is

called the current “cost of goods”: indeed, many put effort into reducing them. Again, however, this ignores the fact that the current market design aims to promote generic and biosimilar competition at the end of the exclusivity period. With competitive market forces, entrants will compete on price, thereby reducing product prices to a point that will sustain competition among multiple entrants, thus, approximating the social marginal cost of manufacturing and distribution (including marketing costs). In other words, as long as the end of exclusivity is enforced and the transition to generic and biosimilar competition promoted, there is really no need to collect information on the cost of goods of specific products. Indeed, using price control to force down the price of the innovator’s product will reduce the incentive for generic and biosimilar company entry. Studies of European markets, where pricing policies impact post-patent markets differently, have shown, for example, “On the one hand, systems that rely on market-based competition in pharmaceuticals promote a clear distinction between firms that act as innovators and firms that act as imitators after patent expiry. Here, original products enjoy premium prices and exclusivity profits under patent protection, and face fierce price competition after patent expiry. On the other hand, in systems that rely on administered prices, penetration by generic drugs tends to be rather limited.” (Maggazini et al., 2004). The “delay request” mechanism in the IRA to allow biosimilar entry and use competition rather than set an MFP (which by implication will make competitive entry harder) supports the view that price control makes entry less attractive for generic and biosimilar manufacturers. The reality is that market competition will generate a market price that approaches the marginal cost of production and distribution. No further negotiation is needed.

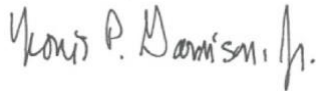
Finally, we would like to re-iterate and emphasize that the key factor that should be considered in Medicare Drug Price Negotiation Program to better align price with value is the “(A) The extent to which such drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives.” Pursuing that objective would provide better incentives that are more likely to promote dynamic efficiency, i.e., the optimal amount and types of R&D investments to improve population health and well-being. In other words, implementation of the legislation should either focus on an MFP linked to value (driven by comparative effectiveness) or an MFP linked to simulating a post-patent/ post-exclusivity market with potential generic or biosimilar entry. In either case, R&D costs are irrelevant, even if they could be appropriately attributed.

Summary Recommendation:

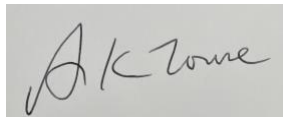
In terms of the implementation of the MFP under IRA, we would recommend: (a) removing any link to use R&D costs to reduce or increase the price derived from the use of comparative effectiveness research; (b) focusing on the estimation of the value that the product is delivering to patients, families, and the health system; (c) avoiding completely the related erroneous notion or calculation of R&D cost “recoupment”; and (d) focusing on ensuring more competitive entry from generic and biosimilar manufacturers.

We appreciate your consideration of our comments as you develop and refine the Drug Price Negotiation Program and its policies. We look forward to continuing to work with CMS to ensure that this program is implemented to promote more efficient development of and equitable access to innovative medicines for all Americans, while producing knowledge that is beneficial for the health and well-being of all persons globally. Please contact us if you have any questions regarding our comments.

Yours sincerely,



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Literature References:

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10 April 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
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Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

GenAdam Therapeutics appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

GenAdam Therapeutics is a platform company using pyroptosis to directly induce tumor cell death and provide anti-tumor immune surveillance. GenAdam's aim is to safely and efficiently deliver a programmed cell death gene (caspase-1) through an adeno-associated virus delivery vehicle for the induction of pyroptosis.

Summary Comments

Provision 30.1

Recommendation

Change the timing for NDA-path negotiations from 9-years to the same 13-year period as for BLA-path drugs. While 13 years is less than the typical 14 years of marketing exclusivity afforded by patent protection, investment can recalibrate slightly to one less year with very slightly higher launch prices so as to keep drug R&D investible.

Provision 30.1.1

Recommendation

The harms from IRA's treatment of orphan drugs could be mostly alleviated by creating small- and large-molecule parity for negotiation at 13 years (see above). CMS should look to only active orphan drug designations for the purposes of determining eligibility for the orphan drug exclusion (not including withdrawn orphan drug designations). Ideally, NDA-path drugs would get 13 years before being negotiated, in which case this provision is harmless. But until then, investors would need to know that if the old generic drug's approvals serve to invalidate the orphan exemption of the new formulation, then CMS would consider the availability of generics to also serve as a basis for not selecting the new formulation for negotiation (at least not until year 11 for price reduction after 13 years). Furthermore, the bona fide marketing standard is extra-statutory in nature with no basis in the law, which defines the standard simply as "marketed". The standard is ambiguous and subjective. The appropriate test, as specified in the IRA, is an objective, point-in-time determination of whether a drug has been "marketed," which can be determined by reference to the

“market date” reported by the manufacturer to the Medicaid Drug Rebate Program. It is defined as the date on which the drug is first sold in the US, and is the standard that CMS is using to determine whether a drug is marketed for purposes of the MDRP, the Part D inflation rebate guidance, and ASP (where the standard is articulated slightly different as the “first sale date.”

Provision 50.2

Recommendation

Provision 90.4

Recommendation

The IRA threatens to make generic business models unsustainable for drugs that treat Medicare populations. One might think this doesn't matter because price reduction will be achieved via negotiation. However, because generic competition often drives costs down not only by eroding the gross margins of the original drug but also spurring manufacturing improvements that lower cost of goods, the IRA threatens to leave society paying more for old drugs in the long run by deterring generic competition. This could increase overall costs across market segments (Medicare and commercial payers).

Provision 40.2.2

Recommendation

* * * * *

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized.

Best regards,

A handwritten signature in blue ink that reads "David Sherris".

David Sherris, Ph.D.
President and CEO
GenAdam Therapeutics

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Phone: (202) 296-7272
Fax: (202) 296-7290

April 14, 2023

Meena Seshamani, MD, PhD
Deputy Administrator
Centers for Medicare & Medicaid Services
Hubert H. Humphrey Building
200 Independence Avenue SW
Washington, DC 20201

Sent via electronic mail

Re: Comments on *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026*

Dear Dr. Seshamani:

Genentech appreciates the opportunity to provide comments on the *Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026* (the “Guidance”). We believe we have aligned goals in seeing the Inflation Reduction Act implemented to reduce patient costs, prudently spend taxpayer funds on needed medicines, and maintain or improve the innovation ecosystem in the United States.

Genentech is a leading biotechnology company dedicated to pursuing groundbreaking science to discover and develop medicines for people with serious and life-threatening illnesses. We are committed to improving patients’ lives through new innovations. To this end, in 2022 we, under the Roche umbrella, invested \$15 billion globally in research and development – more than any other health care company in the world. In the past ten years, we have delivered to patients 20 new medicines that treat devastating diseases like cancer, multiple sclerosis, and hemophilia. In addition to our over 40 approved medicines, we have 70 potential new medicines in clinical or preclinical development and have been granted 39 FDA Breakthrough Therapy Designations for medicines with the potential to provide substantial improvement over currently available treatments.

Access to clinically appropriate treatment is essential to improving health and health equity for Americans. To this end, we provide the following comments and recommendations to help us achieve our shared goals of reducing Medicare spending and patient out-of-pocket costs, while still delivering needed innovations to patients today and in the future. Specifically, in implementing the IRA’s Medicare Drug Price Negotiation Program (the “Negotiation Program”), CMS should:

- **Deliver savings and preserve incentives for innovation.**
 - Convene stakeholder panels to help inform key decision points (e.g., therapeutic alternatives, unmet needs, therapeutic advances, patient and societal benefits) (50.2, 60.3)
 - Establish the maximum fair price (MFP) for products addressing unmet needs or advancing patient care at the ceiling price (60.3)
 - Only consider manufacturer-specific data in instances where the selected drug provides fewer benefits relative to therapeutic alternatives(60.3)
 - Clarify that products will be excluded from the Negotiation Program if they are approved for a sole orphan indication at time of selection, regardless of how many orphan designations the product may have (60)
- **Ensure patient benefit and program integrity.**
 - Establish standards that ensure patients will be, at the very least, no worse off in terms of both access to therapy and cost-sharing, under the Negotiation Program than they were previously (110)
 - Provide meaningful opportunity for patient and stakeholder feedback, including on key decision points and on CMS's analyses (60.3, 40.2.2)
 - Establish retrospective implementation of the MFP via a third party administrator to ensure seamless access to selected drugs (40.4)
 - Implement a system to identify 340B-eligible sales at the point of sale to avoid duplicate discounts (40.4)
- **Use manufacturer-specific data definitions to encompass important aspects of drug development.**
 - To the extent CMS takes into account manufacturer-specific factors, including research and development (R&D) costs, include in the definition of R&D costs the costs of failures from research areas that never had a drug come to market, the cost of ongoing studies, and acquisition costs (of both marketed and failed drug candidates), to include partnering agreements and any other in-licensing development agreement (60.3.4 and Appendix C)
 - Establish agreements with secondary manufacturers of a selected drug to ensure a complete data picture and transparency between CMS and all manufacturers (40)
- **Create a workable exchange of information between manufacturers, stakeholders and CMS.**
 - Establish feasible data submission criteria to enable manufacturers to meet the submission deadline (which is only 30 days after selection), including by allowing rolling submissions of data to inform the initial offer and counteroffers (50.1, 50.2, 60.4)
 - Similarly, allow for a rolling submission of data by the public to ensure CMS has the best data available to inform the negotiation process (50.2)
- **Maintain viability of generic and biosimilar markets.**
 - Remove a drug from the Negotiation Program (i.e., no MFP) if a generic or biosimilar launches after the end of the negotiation period, but before the Initial Price Applicability Year (IPAY) begins (70)
 - Remove requirement for robust and meaningful competition from generic/biosimilar marketing requirement within QSSD definition (90)
- **Ensure public trust and safeguarding of information.**

- Establish robust confidentiality standards to protect manufacturer proprietary information (40.2.1)
- Provide transparency into CMS analyses and evaluations of selected drugs and allow for stakeholder feedback (40.2.2)

For ease of review, we provide our section by section comments in the order CMS provided in the Guidance.

SECTION 40 REQUIREMENTS FOR MANUFACTURERS OF SELECTED DRUGS

CMS should enter into agreements with Secondary Manufacturers to ensure a complete accounting of manufacturer-specific data and allow Secondary Manufacturers to participate in the negotiation process.

When a selected drug has more than one manufacturer, CMS intends to designate each such manufacturer as either the “Primary Manufacturer” or a “Secondary Manufacturer.” The Primary Manufacturer would be the New Drug Application or Biologics License Application holder, and all other manufacturers would be deemed Secondary Manufacturers. CMS intends to require the Primary Manufacturer to carry out all duties relating to the Negotiation Program and does not contemplate any direct relationship between the Secondary Manufacturer and CMS. For instance, the Primary Manufacturer would be required to report aggregated data from both the Primary Manufacturer and any Secondary Manufacturer(s) for non-FAMP, current unit costs of production and distribution, and certain data within market data and revenue and sales volume for the selected drug. However, the Guidance indicates that CMS would consider only those R&D costs incurred by the Primary Manufacturer. Further the Guidance contemplates only the Primary Manufacturer participating in negotiation activities with CMS and, under Section 40.2.2 *Data use, Disclosure, and Destruction*, would prohibit the Primary Manufacturer from sharing any information with Secondary Manufacturer(s), effectively blocking the Secondary Manufacturer(s) from aiding the Primary Manufacturer in negotiating the selected drug’s MFP with CMS.

We have three main objections to CMS’s proposed approach. First, it imposes an undue burden on the Primary Manufacturer by requiring the Primary Manufacturer to collect sensitive information from other manufacturers and report that information to CMS. Second, limiting the consideration of R&D cost data to that only of the Primary Manufacturer does not take a holistic view of the role of each manufacturer in developing a selected drug. Third, the approach does not contemplate any role for Secondary Manufacturer(s) in the Negotiation Program even though Secondary Manufacturers would have information and perspectives worth considering as part of the process.

To address these concerns, we recommend that CMS enter into a Negotiation Agreement with each Secondary Manufacturer pursuant to which:

- The Secondary Manufacturer is required to directly submit information regarding each of the relevant negotiation data elements, which should include R&D costs, directly to CMS, allowing

CMS to obtain needed information without requiring manufacturers to share commercially sensitive information with competitors; and

- The Secondary Manufacturer is permitted to witness all negotiation activities alongside the Primary Manufacturer, including each of the negotiation meetings with CMS, and to access all written correspondence between CMS and the Primary Manufacturer regarding the negotiation process, subject to the data use, disclosure, and destruction requirements described in Section 40.2.2 of the Guidance.

To simplify things for CMS, the agency could draft a single Negotiation Agreement, to be signed by both Primary Manufacturers and Secondary Manufacturers, and clearly delineate which terms are applicable to Secondary Manufacturers, Primary Manufacturers, or both.

Section 40.2 Submission of Data to Inform Negotiation

- a) 40.2.1 Confidentiality of manufacturer submitted data

CMS should work closely with manufacturers to determine a more appropriate and thorough confidentiality and data use policy that will safeguard manufacturer proprietary data.

Section 1193(c) of the Inflation Reduction Act (IRA) restricts both use and disclosure of proprietary data, but in the Guidance, CMS fails to fully articulate its confidentiality policy. Instead, CMS “intends to implement a confidentiality policy consistent with existing requirements for protecting proprietary information, such as Exemption 4 of FOIA...” The lack of detail in this proposed policy raises important concerns about what CMS will consider proprietary, how proprietary information may be used, and how CMS will safeguard the data from unauthorized access, disclosure, or use. At a time where cybersecurity threats and corporate espionage by foreign actors are increasing, particularly within the biopharmaceutical sector, CMS’ collection of such highly sensitive information could leave the government and manufacturers vulnerable to attack.

It is in the interest of all parties to develop a mutually beneficial, comprehensive confidentiality policy concerning the exchange and safeguarding of sensitive information. We therefore urge CMS to propose and open for public comment a detailed confidentiality policy for the Negotiation Program. In doing so, we recommend CMS consider explicitly incorporating reference to trade secret protections, evaluate appropriate FOIA exemptions, and consider modeling its policy on federal and state requirements that have successfully implemented protections for similarly sensitive confidential information.

Additionally, we disagree with CMS’ contention that certain information reported by manufacturers is part of the public record and thus not subject to protection nor exempt from disclosure under FOIA. Indeed, some of what CMS is defining as “federal financial support”—for example, research and development (R&D) tax credits and certain aspects of a manufacturer’s federal grants or contracts—are not publicly available, as CMS asserts. Further R&D costs and program failures for a specific molecule or therapeutic area, net revenue and price calculations, costs of production, information from tax filings, and certain government contracts are proprietary information that are not publicly available. As these data points are all key competitive information, they must be kept confidential and only used for the purposes outlined in the statute. For these reasons, we suggest CMS work closely with manufacturers to determine

a more appropriate definition of confidential information that would not risk public disclosure of confidential information. We further urge CMS to ensure that manufacturers have the opportunity to review any CMS statements or data regarding a selected drug prior to publication to ensure that no proprietary or confidential information can be inferred.

b) 40.2.2 Data Use, Disclosure and Destruction

CMS should revise its data use, disclosure, and destruction policies to reflect important principles of government accountability, free speech, and fair negotiation practices. Further, CMS should make public its analyses (except, as applicable, to keep confidential any manufacturer-submitted proprietary data), and provide an opportunity for public comment.

In the Guidance, CMS describes manufacturer requirements related to the submission of data and the use, disclosure, and destruction of data and other information received during the negotiation process. Specifically, CMS proposes to prohibit a manufacturer from publicly disclosing any information contained in CMS' initial offer, counter offers, or concise justification, as well as any information exchanged during the negotiation period. Further, CMS proposes to require that all CMS information retained by the manufacturer during the negotiation process be destroyed within 30 days of a drug no longer qualifying as a selected drug. CMS believes such requirements will align negotiations under the Negotiation Program with negotiations typically conducted by other entities, and will enable CMS to achieve the lowest MFP for each selected drug. We have several concerns with these proposed requirements.

First, the proposed policies fundamentally contradict the principle of government transparency and accountability. Transparency in how the government conducts negotiations—with careful consideration given to the confidentiality of sensitive manufacturer-provided information, as described above—is critical to the public interest, especially for patients who have the most at stake in the negotiation. Yet under this policy, CMS' analyses and methods for determining an initial offer and evaluating subsequent counteroffers will, at best, be summarized in CMS' concise justification. While some elements of a negotiation between two private entities are similarly subject to a confidentiality agreement, the public sector is unique in its obligation to serve the American people and to be subject to public scrutiny, which forces accountability in how the government is executing the law (and in this case, ensuring that the government is appropriately balancing the important goals of cost reduction and access to both current and future treatments).

Second, CMS justifies its proposal around the use, disclosure, and destruction of data and other information received during the negotiation process as being in alignment “with how negotiations are typically conducted by other entities.” However, the Negotiation Program does not represent a true, open, and voluntary negotiation, considering the penalties for manufacturer noncompliance that apply throughout the negotiation process. Moreover, as a general matter, the confidentiality agreements we enter into with other entities (payers, PBMs, etc.) are the result of mutual negotiation of the terms, and narrowly scoped to offer the minimally necessary protection for each party. In contrast, CMS' proposed policy appears designed to exclusively benefit the Agency in its aim to achieve the lowest MFP, which CMS

itself asserts. Additionally, our private sector agreements do not include any requirements to destroy documentation.

Third, the proposed policies regarding data use, disclosure, and destruction would prevent manufacturers from maintaining institutional knowledge about critical aspects of the negotiation (e.g., information considered and methodologies used) for the purposes of negotiating future selected drugs or renegotiations. Not only does this requirement exceed CMS' authority under the statute, it does not adhere to data retention policies imposed in other federal programs.

In light of these concerns, we strongly urge CMS to revise its confidentiality policy in alignment with the following principles:

- Manufacturers must be able to negotiate the terms of the confidentiality agreement.
- Any restrictions on a manufacturer's use or disclosure of information exchanged during the negotiation process should be narrow.
- CMS should make public its analyses (except, as applicable, to keep confidential any manufacturer-submitted proprietary data), and provide an opportunity for public comment.
- CMS' data destruction policy must be modeled after similar policies used in other federal programs.

Additionally, as discussed above in Section 40, CMS should allow each Secondary Manufacturer to participate in all negotiation activities alongside the Primary Manufacturer, including each of the negotiation meetings with CMS, and to access to all written correspondence between CMS and the Primary Manufacturer regarding the negotiation process. If CMS does not adopt this recommendation, at the very least, CMS must allow the Primary Manufacturer to share any and all documentation regarding the negotiation process with Secondary Manufacturer(s).

Section 40.4 Providing Access to the MFP

CMS should establish retrospective implementation of the MFP via a third party administrator to ensure seamless access to selected drugs. Additionally, to fulfill the statutory obligation to avoid duplicate discounts, CMS should implement a system to identify 340B-eligible sales at the point of sale.

We appreciate CMS' intent to allow manufacturers to offer the MFP to MFP-eligible entities and their providers retrospectively, as it aims to provide manufacturers meaningful flexibility while promoting program integrity. However, as proposed, this option lacks important provisions and safeguards, making it extremely difficult for manufacturers to implement. Specifically, we have the following concerns with the proposed approach:

- A lack of data access to validate MFP eligibility—While manufacturers are required to offer the MFP only to, or on behalf of, MFP-eligible individuals, the Guidance provides no mechanism or process through which data are made available to manufacturers to identify qualifying individuals.
- Insufficient time to provide retrospective reimbursement—When a manufacturer chooses to provide retrospective reimbursement, the Guidance would require the manufacturer to reimburse

pharmacies and intermediaries, including wholesalers, within 14 days. While unclear, we interpret this to mean within 14 days of dispensing (rather than the manufacturer's receipt of an invoice). Regardless, this narrow time frame, paired with the above-mentioned lack of data, does not provide sufficient time for manufacturers to validate MFP eligibility or identify potential duplicate discounts.

- Interplay with 340B—Under section 1193(d) of the Social Security Act (the “Act”), manufacturers are not required to offer the MFP to a provider if the provider was already offered a lower price under the 340B Drug Pricing Program; if the MFP is lower than the 340B price, on the other hand, manufacturers must offer the lower MFP price for that product. Because it can take longer than 14 days to identify a 340B-eligible claim, pharmacies—not knowing at the time of dispensing or claim filing that a claim was eligible for a 340B discount—could invoice manufacturers for the difference between a non-340B acquisition price and the MFP. (Through the typical replenishment model used by pharmacies, however, the dispensed product would have actually been acquired at the 340B price.) Manufacturers in this case could end up paying duplicate discounts when that claim is later identified as 340B-eligible.

To avoid these issues, and to promote program integrity, we urge CMS to:

- Remove the requirement for retrospective payment to be made within 14 days, in recognition of the operational complexities.
- Implement a process akin to the current Coverage Gap Discount Program (CGDP) whereby a third party administrator facilitates manufacturers' access to data in order to identify/validate MFP-eligible claims and facilitate rebate payment. Modeling a solution off of the CGDP could help (but not necessarily resolve) concerns around the very short window for repayment proposed in the Guidance, since the CGDP allows for up to 38 days from report receipt to make payment.
- Implement a system to identify 340B-eligible claims at the point of sale. This system should be paired with strict enforcement of the use of the 340B indicators, as proposed for the Part D inflation rebate Guidance.

SECTION 50 NEGOTIATION FACTORS

Section 50.1 Manufacturer-Specific Data

CMS should revise definitions included in Appendix C to better reflect how companies approach drug development. Additionally, CMS should establish flexibilities in line with statutory requirements for manufacturers to provide basic information by the October 2, 2023 deadline, while extending the deadline for new reporting requirements.

We are very concerned that the manufacturer-specific factors set forth in section 1194(e)(1) of the Act are not reflective of the benefits a product delivers or of how prices are set in a competitive market. Moreover, as evidenced by CMS' proposed definitions for each of the manufacturer-specific factors, and the Agency's proposed approach for using such data, it will be very difficult to establish uniform definitions for these terms, creating the high likelihood that any meaningful reliance on these factors as part of the Negotiation Program would result in an arbitrary determination of the MFP across selected drugs. As discussed in more detail in subsequent sections, establishing price based on benefits provided to

patients and society is key to achieving goals of both reducing costs and maintaining incentives for the highest value treatments. We therefore urge CMS to consider the manufacturer-specific factors outlined in Section 1194(e)(1) of the Act only for those selected drugs that provide fewer benefits than therapeutic alternatives.

To the extent that CMS must apply the manufacturer specific data, the Agency should define, collect, and apply data from all manufacturers of a product. The Guidance contemplates that CMS would consider only certain information from the Secondary Manufacturer(s) as part of the negotiation process. In particular, CMS would consider only those R&D costs incurred by the Primary Manufacturer. We are concerned that this approach does not take a holistic view of the role of each manufacturer in developing a selected drug by limiting the consideration of R&D cost data to that only of the Primary Manufacturer. As stated in Section 40, we recommend instead that CMS enter into agreements with all Secondary Manufacturers and expand data collection from Secondary Manufacturers to include R&D costs.

Additionally, CMS is requesting new price types and cost calculations that are not required under any other government program (e.g., R&D costs by drug or U.S. commercial average net price). New systems and software, data flows, and interoperable connections will need to be established that will require significant investment and can take more than one year to develop and implement. Therefore, the requirement for manufacturers to submit all of this data within 30 days after CMS publishes the selected drug list is very concerning. Under current systems and assumptions, this would not be possible to complete within 30 days because novel accounting practices would need to be developed using data collected from multiple external partners (depending on the selected drug). CMS should use its enforcement discretion to implement procedures such that the submission of certain basic information by the statutory deadline will not trigger penalties, even as the manufacturer continues to supplement the information through a secondary deadline.

The manufacturer specific factors are discussed in more detail in the discussion of Section 60.3.4 and Appendix C, below.

Section 50.2 Evidence About Therapeutic Alternatives for the Selected Drug

CMS should allow submission of data on a rolling basis from all stakeholders and explicitly seek out feedback from patients, caregivers, and clinicians. Further it is essential that CMS accept data submissions after the Agency has established therapeutic alternatives for a selected drug.

Timeline: The timeline for all stakeholders to submit data on the factors enumerated in Section 1194(e)(2) of the Act is too short. We strongly urge CMS to allow for the submission of data on a rolling basis. Additionally, CMS must allow manufacturers and other stakeholders to continue to submit data after CMS has made its selection of therapeutic alternatives public. This is crucial for a valid analysis of a selected drug because the identification of therapeutic alternatives is foundational to the other data CMS will consider under section 1194(e)(2), including therapeutic benefit and comparative effectiveness. (See comments below on Section 60.4).

Solicitation of Evidence: Patients with conditions treated by the selected drug (and their caregivers) and providers treating conditions for which the selected drug is indicated are the most important stakeholders

for the purposes of the Negotiation Program. As such, they should be offered the opportunity to engage with CMS beyond simply providing written comments 30 days after a product is selected for negotiation. The ICR is restrictive (in both scope and time to respond) and not conducive to robust participation by these stakeholders, especially those less familiar with, and with fewer resources to commit to, engagement with the federal government. CMS should explicitly seek out their feedback, ideally by identifying and proactively engaging the stakeholders most affected, or with the most experience in the given therapeutic area. Engagement of these stakeholders should occur in public fora and should allow for a more open exchange (vs. one-way ICR process). Feedback provided by these two important groups should be given higher priority than other comments from the public. Three major areas where their feedback should be solicited are:

- **Unmet needs:** What are (or were previously) unmet needs for their conditions? Or the conditions they treat? And the extent to which a selected drug may (or may not) meet these needs across a drug's lifecycle?
- **Therapeutic alternatives:** What are appropriate therapeutic alternatives to the selected drug? Specifically, what products would you feel comfortable being treated with (or using to treat) instead of the selected drug? How do alternatives compare to the selected drug in terms of safety, efficacy, and quality of life?
- **Therapeutic advance:** What represents a therapeutic advance for a specific indication? And the extent to which a selected drug may (or may not) provide such advancement? To what extent the selected drug substantially improves treatment of Medicare beneficiaries?

SECTION 60 NEGOTIATION PROCESS

In creating and implementing the IRA's Negotiation Process, CMS should both produce savings and preserve incentives for innovation. The MFP methodology should help incentivize investments in the types of treatments that have the most potential for patients. Specifically, 1) CMS should establish the MFP at the ceiling price for products that address unmet needs or are proven to be therapeutic advances, and 2) only use the manufacturer-specific data to adjust the initial offer if the product provides fewer benefits than therapeutic alternatives.

The IRA directs the Secretary to develop and use a consistent methodology and process for negotiations that aims to achieve the lowest maximum fair price (MFP) for each selected drug, and requires the Secretary to consider nine enumerated factors, *as applicable* to the relevant selected drug, as the basis for determining the MFP offers and counteroffers. At a principal level, we believe that CMS should implement the IRA to achieve two overarching and equally important goals: 1) delivering cost savings to Medicare and its beneficiaries, and 2) maintaining incentives to invest in the innovations that can deliver meaningful benefits to patients. We urge CMS not to overlook the crucial nature of the latter – to achieve this, it is critical that CMS create a process that predictably recognizes therapeutic advances and treatment options that address unmet medical needs by weighting benefits to patients and society most heavily, and only considering manufacturer-specific data in cases where there is no evidence of such benefits.

In establishing this patient-centered framework, CMS should explicitly define evidence standards for demonstrating therapeutic advance and unmet need and how that evidence will be translated into the initial MFP offer in order to create a predictable paradigm. Evidence standards should incorporate

feedback from stakeholders, particularly patients, caregivers, and providers, to ensure that the standards are meaningful to Medicare beneficiaries and those who care for them. A predictable and meaningful pricing system is key to incentivizing investment in the types of therapies that are valued most highly. Without a system that clearly defines and predictably recognizes therapeutic advances and products addressing unmet medical needs, we anticipate that investment¹ will move away from the riskiest and most needed research and development efforts. We anticipate products that are structurally disadvantaged under the IRA (e.g., small molecules, products with large Medicare populations, therapeutic areas that require incremental innovation, new platform technologies that require more time for uptake) will be the most affected, with post-approval research and development dollars declining and manufacturers making difficult decisions with regard to US launches (e.g., hold early launches until data on larger patient populations are mature). All of these potential consequences would hurt patients, particularly Medicare beneficiaries. We believe it is possible to achieve a better balance. Below are suggestions specific to CMS' initial Guidance.

We appreciate CMS outlining a methodology to develop an initial offer in the Guidance (Section 60.3). However, as discussed, CMS' proposed methodology does not provide the framework necessary to incentivize the most difficult and riskiest research and development efforts. In order to deliver cost-savings and support innovation, we recommend CMS amend the MFP methodology to:

- Establish an MFP at the ceiling price for products that, over the course of the product's lifecycle, have provided **therapeutic advancements** or treated previously **unmet medical needs**.
 - While the MFP is determined only after a selected drug has been on the market for at least 7 or 11 years, it is essential that a selected drug be recognized for its attributes over the course of its lifecycle to encourage continued innovation. If CMS were to examine the benefits a product provides only at the time CMS establishes the initial MFP offer—which will occur at least 7 or 11 years after the product's initial approval and potentially decades after the initial research investment—manufacturers could not reliably invest in addressing unmet needs and potential therapeutic advances. Specifically, such a methodology would consider the availability of products that were approved well after the manufacturer decided to invest in the development of the selected drug, and arbitrarily fail to recognize the particular value of groundbreaking products in a therapeutic area.
- Create clear criteria for determining whether a product has provided therapeutic advancements or treated previously unmet medical needs over its lifecycle. Specifically:
 - A selected drug would be deemed a **therapeutic advance** if one or more of its indications represents:
 - Significant improvement in clinical outcomes, as assessed by patients with lived experience with the disease. For purposes of this analysis, CMS should establish a standard similar to the *substantial clinical improvement* criterion used by CMS to determine eligibility for the New Technology Add-on Payment (NTAP); OR

¹ Investment includes capital from manufacturers but is also much broader, including capital from venture capital funds and the limited partners typically funding them, public investors, and personal investors.

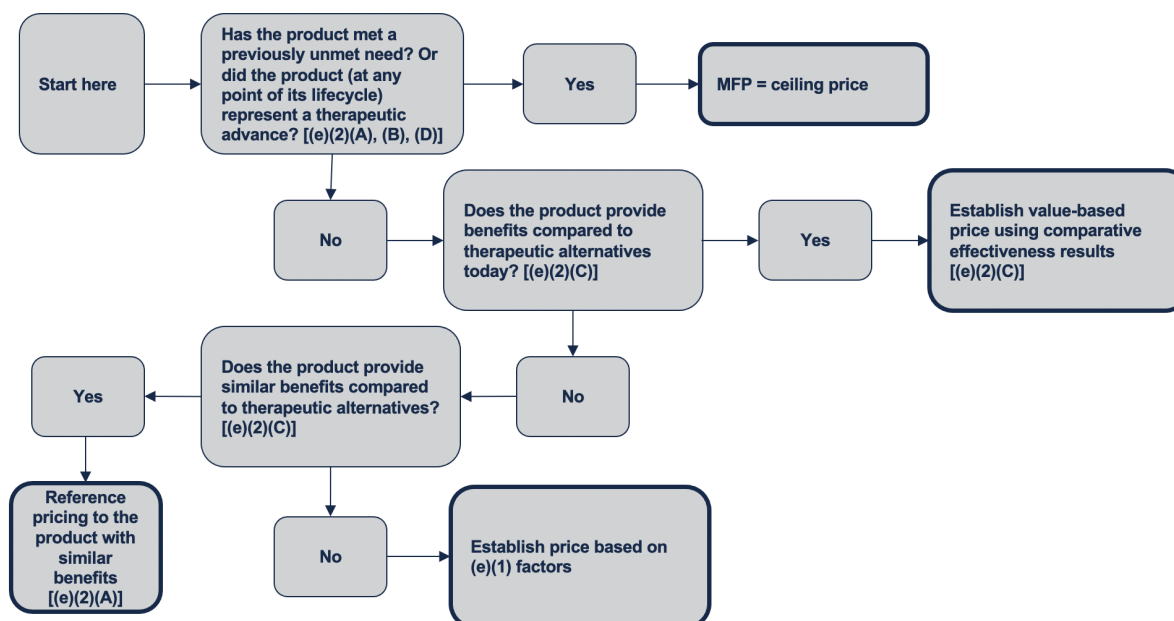
- Improvements on a validated *clinical outcome assessment*,² for the disease state; OR
 - Measurable positive impact in vulnerable populations (e.g., socially vulnerable or disadvantaged, low socioeconomic status, disabled) that could help improve health disparities.
- A selected drug would be deemed to have met a previously **unmet medical need** if one or more of its indications:
 - Was approved to meet an unmet medical need as defined by FDA in its 2014 Guidance³; OR
 - Treats a patient group previously unresponsive to or ineligible for currently available treatments; OR
 - Targets a disease state affecting a disproportionate share of vulnerable patients (i.e., socially vulnerable or disadvantaged, low socioeconomic status, disabled).
- For selected drugs that do not meet one or both of the above criteria, CMS would establish the MFP by considering evidence regarding the **comparative effectiveness** of the drug to determine whether the selected drug provides benefits compared to therapeutic alternatives. In determining the magnitude of benefit, CMS should weigh indications where the selected drug provides benefits compared to existing treatments most heavily. Providing higher weight to indications delivering the most value would help incentivize the most promising drug development (particularly post-approval) and would help remove some disincentives / structural disadvantages created under the IRA for orphan products where research and development can be most difficult and expensive but potential for delivering meaningful benefits may be higher.
- To avoid unintended consequences of setting MFPs too low, CMS should only use the manufacturer specific factors, enumerated in Section 1194(e)(1) of the Act, when a product provides fewer benefits than therapeutic alternatives.

To illustrate how CMS would apply these standards in practice, we have put together the following diagram that contemplates the methodology as a decision tree.

² National Center for Biotechnology Information. Definition and Resources on Clinical Outcome Assessments. Accessed: <https://www.ncbi.nlm.nih.gov/books/NBK338448/def-item/glossary.clinical-outcome-assessment/>

³ US Food and Drug Administration. Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. May 2014. Accessed: <https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf>

Figure 1. Decision Tree to Represent Recommended Methodology for Developing an Initial Offer



This methodology would achieve the following:

- Maintains innovation incentives by establishing the MFP at or near the ceiling price for the highest value products;
- Weights clinical benefits most heavily; and
- Provides savings to Medicare and patients by using prices below the statutory ceiling price for products that demonstrate lower patient value.

While the statute directs CMS to develop and use a consistent methodology for MFP negotiations that aims to achieve the lowest MFP, the statute also requires CMS to take into account the statutory factors “as applicable to the drug,” and gives CMS significant discretion regarding the design of this methodology. The methodology outlined above is consistent with the statute’s broad framework because it can be applied consistently across selected drugs and aims to achieve the lowest MFP while also taking into consideration the statutory negotiation factors “as applicable to the drug.” Specifically, our recommended methodology considers all of the statutory factors and applies them, as applicable, to selected drugs in order to achieve the overarching aims of reducing costs and maintaining access to innovative medicines today and in the future.

Technical clarification needed regarding the orphan drug exemption

CMS should apply the orphan drug exclusion based solely on those orphan drug designations for which a product has approved indications.

Some of the most difficult to treat and highest unmet needs are found in rare diseases, where there are unique challenges for drug development. The IRA’s orphan drug exemption is limited in scope and applies only to those orphan products for which all approved indications treat a single rare disease or condition. However, in the Guidance, CMS has adopted an interpretation under which a product would

lose eligibility for the orphan drug exclusion upon receipt of a second orphan drug designation, regardless of whether that designation has any approved indications. This interpretation creates significant disincentives for orphan drug development.

Orphan drug designations are typically granted early in the development process and provide manufacturers with important incentives (tax credits, exemption from user fees, and potential for longer exclusivity period) to undertake this high-value research. However, an orphan designation does not mean that a product will be successful in being approved for any indications for the designated disease or condition. Indeed, orphan drugs are often studied for multiple disease categories, because of the risk/benefit profile for such research. In other words, drug candidates are studied for multiple diseases to improve their chances of success in obtaining at least one approval. As of April 2023, the FDA has granted 6,445 orphan designations and approved 1,130 orphan indications; these data speak to the risky nature of orphan drug development. And of those designations that ultimately result in an approval, the average time between designation and approval is 65 months or 5.4 years.

Instead of supporting this type of research, CMS' interpretation that a drug with multiple orphan drug designations immediately loses eligibility for the orphan drug exemption undercuts this policy by discouraging manufacturers from undertaking additional research for orphan indications before the manufacturer has any, even remote, certainty that they will be successful in bringing that indication to market. Ultimately this policy will result in less research and progress for patients with some of the highest unmet needs; therefore, we urge CMS to instead clarify that the agency will consider only those orphan drug designations for which a product has an approved indication in applying the orphan drug exclusion.

Section 60.1 Establishment of a Single Proposed MFP for Negotiation Purposes

CMS should provide alternative options for comparing prices between therapeutic alternatives when a 30-day supply is not easily defined or the comparison of the cost of 30-day supplies would be different than comparing the total cost of a course of therapy.

For the purposes of determining a single price included in an initial offer and evaluating clinical benefit compared to therapeutic alternatives, CMS proposes to identify a single price for a 30-day equivalent supply of a selected drug, which is to be weighted across all dosage forms and strengths.

While we understand CMS' rationale for determining a single price for the purpose of negotiating a single MFP, we believe the proposed methodology can be problematic when it is used for cross-product comparison. We believe CMS should be most concerned with the total cost for a similar outcome. Therefore, if comparing a 30-day supply vs. comparing the total cost of a course of therapy would provide different results, CMS must provide alternative mechanisms for comparing price to ensure a fair comparison. Specific examples where problems could arise include (but are not limited to): fixed duration course of therapy, less frequent dosing, differences in dosing for varying indications, differences in persistence and adherence, and differences in loading and maintenance doses.

Before finalizing its approach, we urge CMS to explore, and seek public feedback on, alternatives that will better account for these differences.

Section 60.3 Methodology for Developing an Initial Offer

a) 60.3.1 Identifying Indications for Selected Drug and Therapeutic Alternatives for Each Indication

CMS should identify preliminary options for therapeutic alternatives based on rigorous criteria and then convene a multi-stakeholder panel, including patients and clinicians with first hand experience, to validate therapeutic alternatives for each indication. At the conclusion of this process, CMS should make the selection of therapeutic alternatives public and accept additional data submissions from all stakeholders.

CMS intends to identify all labeled indications from the products prescribing information and identify therapeutic alternatives for each indication using data submitted by the Primary Manufacturer and the public, FDA- approved indications, indications included in the CMS-approved Part D compendia, widely accepted clinical guidelines and peer-reviewed studies. CMS intends to begin by identifying therapeutic alternatives within the same drug class as the selected drug based on properties such as chemical class, therapeutic class, or mechanism of action (MOA) before considering therapeutic alternatives in other drug classes. We support CMS' intent to identify therapeutic alternatives by indication and to start with products with the same MOA. As such, we recommend that to identify the preliminary options for therapeutic alternatives, CMS should look to evidence-based clinical guidelines and other widely recognized, scientifically rigorous, evidence-driven resources to identify preliminary therapeutic alternatives. CMS should prioritize products with the same mechanism of action (MOA) and the same indication / labeled populations to identify therapeutic alternatives. If a product is the only one of its MOA for a given indication, it should be viewed as not having any therapeutic alternatives, unless an evidence synthesis demonstrates the same or better outcomes with another treatment for the given indication. If in evaluating comparative effectiveness research, a selected drug has significant improvements compared to a potential therapeutic alternative, the product should not be included as a preliminary therapeutic alternative.

After CMS has identified preliminary therapeutic alternatives, CMS should convene a multi-stakeholder panel (explicitly including manufacturers, patients with lived experience [including patient advocacy groups], and clinicians treating the conditions in question) in order to validate the correct therapeutic alternative(s) for each indication. Ideally this process should consider both quantitative and qualitative data as well as input from patients and clinicians, as not all of the ways that treatments impact patients can be routinely captured and compared quantitatively. Finally, CMS must make a public determination of therapeutic alternatives as early in the process as possible to allow sufficient time for the manufacturer to submit additional data and prepare for any potential counter offers.

b) 60.3.2 Developing a Starting Point for the Initial Offer

CMS should be agnostic to whether the starting price is above or below the ceiling price as the statute only limits offer and counteroffers at the ceiling price. CMS should not penalize products with no therapeutic alternatives by using a different pricing metric for the starting point.

For selected drugs with at least one therapeutic alternative, CMS intends to use the net price(s) and/or ASP(s) of such therapeutic alternative(s) as the starting point for the initial offer. To the extent a selected drug does not represent a therapeutic advance or address an unmet need and thus qualify for an MFP at the ceiling price (see Figure 1), we support the use of net prices and/or ASPs as the starting point for the initial offer. However, we are concerned that CMS intends to cap the starting price at ceiling price. The statute requires only that CMS cannot make an initial offer or accept a counteroffer that is below the statutory ceiling price. Limiting each step of the pricing methodology at the ceiling price would arbitrarily cap intermediate prices, depressing the amount CMS subsequently adjusts both upwards and downwards based on the various statutory negotiation factors. CMS should instead use the therapeutic alternative pricing as the starting point regardless of whether it is above the statutory ceiling price. CMS can then apply the statutory ceiling price as the last step in the process.

Additionally, for selected drugs without therapeutic alternatives, CMS intends to use the Federal Supply Schedule or Big Four price as the starting price. We disagree with CMS' intended policy to use the FSS or Big Four price for selected drugs with no therapeutic alternatives, as this price is artificially depressed through the inclusion of certain required discounts. This seems particularly inappropriate for products for which there are no other therapeutic options. For these products, the starting point should instead be the product's own net price or ASP.

c) 60.3.3 Adjusting the Starting Point based on Clinical Benefit

CMS should create comparative clinical effectiveness standards, by which it adjusts the starting point upwards or downwards, based on the totality of quantitative and qualitative evidence with special recognition of input from those directly affected by the disease state or treatments being evaluated. Further, CMS should use FDA's well established definition of unmet need to better recognize important treatment advancements.

Comparative Effectiveness Research: In this section the agency states, "To evaluate the clinical benefit conferred by the selected drug compared to its therapeutic alternative(s), as applicable, CMS intends to broadly evaluate the body of clinical evidence, including data received from the public and manufacturers as described in section 50.2 of this memorandum, and data identified through a CMS-led literature review. CMS may also analyze Medicare claims or other pharmaceutical drug datasets for utilization patterns, clinical data, or other information relevant to the selected drug and its therapeutic alternative(s) and may consult with clinical and academic experts." We agree with CMS' general approach, but would also recommend that the agency incorporate the following:

- CMS should create comparative clinical effectiveness standards such that CMS compares the totality of evidence of the impact of treatments on patients, their families/caregivers, the health system and society overall. To do this, CMS should convene a panel of patients, caregivers, and clinicians to provide input on the disease state and treatment options. *This recommendation builds on recommendations provided in Section 50.2 regarding stakeholder convening.*
 - A holistic approach to comparative clinical effectiveness is required because formal comparative clinical effectiveness methods have a rigid focus on regulatory endpoints that change over time and ignore the highly important patient-relevant and health system-related treatment factors that drive overall patient outcomes.

- To do this, in addition to information collection described in Section 50.2, CMS should convene panels of patients and providers with lived experience with the products and disease states being evaluated. CMS should limit stakeholder feedback that is not tied to published studies or guidelines to those with first hand experience.
- For selected drugs with multiple indications, CMS should weight indications where the selected drug provides benefits to patients most heavily. This will help provide incentives for manufacturers to invest in the most promising assets and incentivize post-approval R&D efforts for the most promising indications.
- When analyzing real world evidence (RWE) (or evaluating completed RWE studies) to determine treatment effects, CMS must use methods that are anchored to best practices for defining patient progression or outcomes or leverage validated methods in peer-reviewed literature.

Unmet need: In this section, the agency states, “CMS will consider whether the selected drug fills an unmet medical need, which CMS intends to define as treating a disease or condition in cases where very limited or no other treatment options exist.” This definition is far too narrow and does not adequately contemplate the needs of patients with serious conditions and how drug development aims to meet unmet needs. As stated above, we recommend CMS adopt the following standards for “unmet medical need”:

- A product approved to meet an unmet medical need as defined by FDA in its 2014 Guidance⁴;
OR
- Treats patient group previously unresponsive to or ineligible for currently available treatments;
OR
- A product targeting a disease state affecting a disproportionate share of vulnerable patients (i.e., socially vulnerable or disadvantaged, low socioeconomic status, disabled).

Weighting of Indications: We appreciate CMS’ call out that benefits may vary depending on indication and that a qualitative approach to adjustment may be necessary. We want to reiterate the importance of weighting indications with greatest patient or societal benefits most heavily. This will help incentivize drug development activities that have the most promise to advance patient care.

d) 60.3.4 Consideration of Manufacturer-Specific Data

CMS should only consider manufacturer specific data when a product provides fewer benefits compared to therapeutic alternatives.

As noted above, the manufacturer-specific factors do not accurately reflect a functioning drug development market. Drug development is an inherently risky endeavor. Continued robust R&D investment leading to advancements that address unmet need requires a predictable paradigm that is decoupled from the extent to which R&D costs are ultimately recouped. By contrast, defining R&D costs at the level of a single selected drug does not capture the full scope of risk taken in drug development (e.g., failed research targets, partnerships, acquisitions), nor accurately reflect the fluid nature and costs of R&D and drug development over time (e.g., from inflation, natural disasters, supply chain disruptions, or

⁴ US Food and Drug Administration. Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. May 2014. Accessed: <https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf>

investments in manufacturing technology and capacity, etc.), resulting in an incomplete picture of the full costs of R&D. We further note that CMS' current definition for R&D costs is plagued by selection bias in that, by definition, any drug selected for negotiation was a "success". CMS' proposal to consider only the R&D costs of "successes" or therapeutic areas with an eventual success introduces bias to R&D cost factors such that it cannot provide information from which reliable conclusions can be made.

While we recognize that CMS is required by statute to consider all of the statutory negotiation factors, including R&D costs, as applicable to the drug, the inherent flaws in the manufacturer-specific factors militate in favor of prioritizing the clinical factors as part of the negotiation process. Only after CMS determines that a drug does not provide additional benefits compared to therapeutic alternatives should the manufacturer-specific factors be used to inform the initial offer. To prepare for that eventuality, we share the following concerns with CMS' proposals to consider the manufacturer-specific factors:

- CMS intends the manufacturer-specific data to have either upward or downward pressure on the initial offer, but does not clearly describe the circumstances nor the extent to which these data will influence the offered price. Without a clear process, there exists the high possibility for arbitrary application of these data to inform MFP offers.
- CMS suggests that tax credits should be included in calculations of Prior Federal Support. However, the inclusion of tax credits is inconsistent with their intended purpose -- incentivizing behavior to advance an issue of importance to the government, for instance medical innovation. Applying punitive measures to recipients of such tax credits, in the form of downward adjustments, will only slow the innovation these tax credits were meant to encourage.
- Patents and exclusivities award innovation by providing a time-limited opportunity to market a product without certain types of competition – a practice that is enshrined in the Constitution. Manufacturers continue to innovate through continued R&D on approved drugs to show efficacy in additional indications, improve delivery, or improve efficacy. All of these activities, to the extent they result in new intellectual property, may result in new patents or exclusivities. CMS' suggestion that downward pressure on the initial offer may occur if existing patents will "last for a number of years" after drug selection fails to recognize that these patents were awarded to recognize significant innovation, and will be a strong disincentive to continue to innovate after initial approval because the full value of innovation would not be realized.
- CMS is requesting certain price information and states there may be downward pressure on price if the average commercial net price is lower than the ceiling price. What is particularly concerning is that CMS is requesting average commercial price information net of patient assistance, suggesting that CMS intends to treat patient assistance programs as some form of price concession. Collection of price types that are net of patient assistance programs is inconsistent with statute and recent court rulings affirming that patient assistance is meant for patients and is not part of the sales price to purchasers.⁵ Patient assistance programs are not even considered or discussed when developing contracting strategies with commercial entities, further illustrating that patient assistance is not and should not be viewed as a price concession. Therefore, this information is not appropriate to consider when setting the initial price point and we recommend that CMS withdraw these metrics.

⁵ *PhRMA v. Becerra*, Civil Action 1:21-cv-1395 (CJN) (D.D.C. May. 17, 2022)

Additional concerns regarding the arbitrary nature of the definitions of these factors are included below in comments on Appendix C.

Section 60.4 Negotiation Process

CMS must allow for a more dynamic exchange between the Agency and manufacturers during negotiation.

Timeline for submitting data: As discussed with the timeline for submitting data regarding the manufacturer-specific factors described in section 1194(e)(1) of the Act, we are very concerned with the requirement that manufacturers must submit **all** information on the factors described in section 1194(e)(2) to CMS by October 2, 2023, just 30 days after CMS publishes its list of selected drugs. The breadth and complexity of the data that manufacturers are required to report under section 1194 cannot be overstated. This aggressive timeframe will limit the amount of information we can prepare and submit, and it ignores the reality that new information and data—which can be material to the negotiation—are constantly being generated and may not be available in this very short timeframe.

In addition, development of a given drug continues throughout its lifecycle, as new indications, dosages, and formulations are explored and added, bringing meaningful value to patients. Manufacturers collect and publish evidence on a drug’s safety and efficacy over time, which can be particularly important for fixed duration therapies or others whose data on the long-term durability of effect may increase over time. Health economic and outcomes research and other data generated through real-world studies also provide meaningful information about how the drug works in certain populations and settings. As such, CMS can expect that the evidence package for a drug may evolve over the course of the drug selection and negotiation processes. Manufacturers should be able to submit all data, as they become available, that support the most complete and timely characterization of the value of the product.

Finally, CMS notes that it “may also analyze Medicare claims or other pharmaceutical drug datasets for utilization patterns, clinical data, or other information relevant to the selected drug and its therapeutic alternative(s) and may consult with clinical and academic experts” when evaluating the clinical benefit of a selected drug. We are concerned that under CMS’ interpretation of section 1193(a)(4), manufacturers would not be able to respond to or refute CMS’ analyses with the manufacturer’s own data. Additionally, this interpretation also prevents manufacturers from providing any supplemental or clarifying information CMS may request throughout the negotiation process. We disagree with this approach.

Manufacturers must have the opportunity to submit data regarding the section 1194(e)(2) factors after the 30-day timeline described in the Guidance, on an ongoing basis as the data are available. Doing so will: 1) ensure that CMS has the timeliest information to inform its initial offer and subsequent consideration of counteroffers, as applicable; 2) allow manufacturers to respond to or validate CMS’ own analyses; and 3) allow manufacturers to respond to CMS requests, as needed. We believe Congress did not intend to impose such a rigid timeline, nor categorically exclude important product information from CMS’ consideration, as evidenced by the language in sections 1194(a)(2)(A) (as amended by section 1191(d)(5)(A)) and 1193(a)(4)(B) of the Act, which require manufacturers to submit “information that the Secretary requires to carry out the negotiation”—not, for example, “all information to be considered by

CMS during the negotiation process” by the October 2 deadline. Further, Congress did not specify that additional information cannot be submitted after the deadline. CMS, acting in the public interest, should accept and consider all manufacturer-provided data relevant to the negotiation, provided at any point during the negotiation process.

Mechanics of the negotiation process: In this Guidance, CMS proposes a negotiation process that allows for a maximum of three in-person or virtual meetings, two at the request of CMS and one at the request of the Primary Manufacturer of the selected drug. This proposal is overly restrictive—especially considering the length of the negotiation process and the amount and complexity of information to be considered. We recommend CMS instead provide for a more dynamic exchange. Importantly, manufacturers should be able to request meetings after the submission of information regarding the manufacturer-specific factor, but before CMS’ initial offer, and on an ongoing basis to discuss additional information the manufacturer and/or the public may submit to CMS regarding the factors described in sections 1194(e)(1) and 1194(e)(2) on a rolling basis (in alignment with our recommendations above).

SECTION 70 REMOVAL FROM THE SELECTED DRUG LIST BEFORE OR DURING NEGOTIATION

CMS should only require implementation of MFPs for products that remain single source on the first day of the IPAY.

The IRA allows for negotiation only of those products that have been on the market for a specified period of time without a marketed generic or biosimilar. Section 1192(e)(1) of the Act defines a “negotiation eligible” drug as a “qualifying single source drug” (QSSD) “with respect to an initial price applicability year.” The statutory language tying a QSSD to a given IPAY can be read to indicate that, in order to be negotiation eligible for a given IPAY, a product must meet this criterion on the first day of the IPAY, rather than the last day of the negotiation period, as CMS states in the Guidance. Based on this reading, we urge CMS to revise its guidance to more closely follow the intent and text of the statute, which provides that a negotiation-eligible drug ceases to qualify as a QSSD and thus cannot be a selected drug subject to an MFP if a generic or biosimilar enters the market before the first day of the IPAY. For example, for IPAY 2026, if a generic or biosimilar for a negotiation-eligible drug included on the selected drug list comes to market after the end of the negotiation period, but before January 1, 2026, CMS should not apply the MFP for that product during IPAY 2026.

SECTION 90 MANUFACTURER OVERSIGHT AND COMPLIANCE

CMS should not implement a robust and meaningful competition standard for determining whether a product is a QSSD, as it is contrary to the statutory definition.

The statute defines a QSSD as a product without a marketed generic or biosimilar, among other requirements. In determining whether a product has a marketed generic or biosimilar, we appreciate that CMS would want to investigate whether the generic or biosimilar is truly offered for sale and thus a bona fide marketing standard may be appropriate. However, CMS has exceeded the bounds of the statute by proposing to establish a “robust and meaningful competition” standard and to impose requirements that the product be “widely available” or show up in the PDE data. We strongly urge CMS to focus on the

statutory standard of whether the generic or biosimilar is marketed and not to adopt these standards that exceed CMS' authority under the statute.

SECTION 110 PART D FORMULARY INCLUSION OF SELECTED DRUGS

CMS should implement safeguards to preserve access (formulary placement and cost-sharing) to both selected and non-selected drugs after the MDPNP takes effect.

We support the agency's goal of ensuring that selected drugs are covered under Part D; however we have concerns about *how* these products may be covered, and the consequences for patients. When it comes to access to needed treatment, no patient should be worse off under the Negotiation Program than they are today. This principle must be true for all patients, including those taking selected drugs and those taking non-selected drugs. However, as currently constructed—particularly considering the steep discounts CMS is poised to secure through the Negotiation Program and the requirement for selected drugs to be guaranteed coverage under a plan's formulary—the Negotiation Program will fundamentally alter class-wide dynamics for both selected and non-selected drugs and potentially threaten patients' access to needed treatments

Under the current system, manufacturers often offer rebates to plans in exchange for preferred formulary placement. In some therapeutic classes, such rebates are very common and serve as a considerable source of revenue for plans. In these classes, we can expect that the coverage requirements under the Negotiation Program could dramatically reduce plan revenues for that product by requiring plans to cover drugs with a lower price, making it more difficult for plans to negotiate a rebate or other discount. To counter this downward pressure on plan revenues, a plan may nominally include a selected drug on its formulary—thereby technically complying with the statutory requirement—while implementing utilization management techniques (e.g., step therapy) that adversely affect patient access to the selected drug.

Conversely, patients taking non-selected drugs could be worse off than today under two scenarios: 1) generally, as plans face increased liability under the Part D benefit beginning in 2025, they are likely to restrict access (via increased utilization management and/or higher patient out-of-pocket costs) for non-selected drugs, for which coverage is not required, particularly in classes where steep rebates are less common; and 2) if CMS requires that selected drugs have preferred formulary status, patients taking non-selected drugs would likely face utilization management and/or higher patient out-of-pocket costs.

We urge CMS to provide additional specificity around the requirements for coverage of both selected and non-selected drugs, and in doing so, implement safeguards to ensure that plans cannot disrupt care for patients or otherwise make them worse off than under current formulary guidelines. This also underscores the importance of careful consideration of therapeutic alternatives and negotiation of reasonable MFPs for selected drugs, so as not to exacerbate these dynamics.

APPENDIX C DEFINITIONS FOR PURPOSES OF COLLECTING MANUFACTURER SPECIFIC-DATA

CMS must amend definitions of the manufacturer specific data requirements to better realize the realities of drug development.

Appendix C provides CMS' definitions for the manufacturer-specific data being requested. While we believe manufacturer-specific data should only be considered when the selected drug provides fewer benefits than therapeutic alternatives, it is still important that CMS provide clarity, where possible, on what is expected, while recognizing that a one-size-fits all approach will not be possible for all of the requested data points.

Below we address specific comments on each data point.

R&D Costs:

- Generally it is very difficult to apportion R&D costs to just one drug. Because each drug's development path will have unique nuances, R&D costs should include the underlying or fundamental research that enabled, contributed to, or led to the development of the successful selected drug. CMS should also allow manufacturers to make reasonable assumptions on costs and the apportionment of those costs. For example, rather than set an arbitrary limit on length of pre-clinical research to 52 months, CMS should allow manufacturers to make reasonable assumptions on the length of a particular pre-clinical program.
- The definitions proposed by CMS do not reflect how the industry operates with respect to its approach to R&D. Due to the inherent risk in drug development manufacturers will purposefully diversify risk across the entire portfolio and then cross-subsidize over different therapeutic areas or mechanisms of action. The drug development successes enable further research and allow manufacturers to take risks that may never pan out. It is important to remember that the areas of most unmet need are often some of the riskiest areas to develop medicines (e.g., Alzheimer's disease). Therefore, we feel strongly that R&D costs and failures should include the costs of failures from research areas that never had a drug come to market.
- Moreover, the cost of drug development should include the cost of failures because failures are an inevitable consequence of: (1) the pursuit of treating diseases of increasing complexity, and (2) the nature of a scientifically-regulated industry, where the bar for "success" continually rises as improved products come to market. Not counting failures would incentivize the pursuit of "me-too" medicines which might carry the highest likelihood of clinical success, but do the least to advance patient outcomes.
- Secondary Manufacturer R&D costs, including failures, should be included in the calculation of total R&D costs. Excluding these costs would not encompass the full range of drug development scenarios resulting in an inaccurate reporting of the true cost of drug development. For example, Secondary Manufacturers can incur certain R&D costs that will later be used to support the Primary Manufacturer's NDA/BLA filing.
- Drug development takes many paths and may include partnerships or acquisitions that may bring needed funding to support continued development, bring new capabilities or efficiencies, enhance efforts to scale up production, or any number of added benefits. Ultimately this activity furthers advancements in science that can bring innovative drugs that address unmet needs to market. For these reasons, acquisition costs (of marketed and failed drug candidates), partnering agreements, or any other in-licensing development agreement should be included in R&D costs.

- Manufacturers continue to study and innovate on marketed drugs that result in additional R&D costs (e.g., by confirming efficacy in new indications). Given that CMS intends to use R&D costs to place upward or downward pressure on the initial price offering, CMS should allow manufacturers to include the cost of *ongoing* studies (including pre-clinical studies) in their R&D cost calculations to reflect the reality of continued study on marketed drugs. Without including ongoing R&D costs, manufacturers would be disincentivized from conducting further studies as these R&D costs will not be able to inform MFP in those scenarios where the selected drug provides fewer benefits than therapeutic alternatives.

Current Unit Costs of Productions and Distribution:

- As discussed previously, this point-in-time calculation of unit costs of production and distribution do not accurately reflect the true costs since market approval, but rather a snapshot of the current environment at the time of drug selection.

Prior Federal Financial Support:

- As discussed previously, tax credits should not be included in this metric because it is antithetical to the spirit of tax credits generally and would disincentivize the very behavior the tax credit is intended to promote.

Market Data and Revenue and Sales Volume Data:

- CMS is requesting data on new price types not required to be reported under other federal reporting requirements. As stated previously, requesting these price types net of patient assistance is inappropriate and inconsistent with statute as patient assistance is not a form of price concession or remuneration and does not factor into the contracting decisions made by manufacturers.
- CMS should clarify if the new price types being requested should include U.S. Territories to avoid confusion and facilitate accurate price reporting.
- CMS should provide further guidance on how to calculate WAC at the NDC-9 level. WAC is currently calculated at the NDC-11 level and calculations of WAC at the NDC-9 level may require manufacturers to make reasonable assumptions on the methodology.
- CMS should clarify that prices reported for the FSS and Big Four Price are inclusive of the Industrial Funding Fee to remain consistent with the public reporting by the VA.

We welcome the opportunity to discuss these ideas with you further and address any questions you may have. Please reach out to me or Valerie Reynolds (reynolds.valerie@gene.com) at anytime.

Sincerely,



David Burt
Executive Director
Federal Government Affairs
david.burt@gene.com

April 14, 2023

Via email (IRAREbateandNegotiation@cms.hhs.gov)

Dr. Meena Seshamani
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Dr. Seshamani:

Gilead Sciences, Inc. (Gilead) appreciates this opportunity to comment on the above-captioned memorandum providing initial guidance (Initial Guidance) regarding the implementation of sections 11001 and 11002 of the Inflation Reduction Act (IRA), which establish the “Medicare Drug Price Negotiation Program” (MFP Program) to determine “maximum fair prices” (MFPs) for selected drugs.¹

Gilead is a research-based biopharmaceutical company that discovers, develops, and commercializes innovative medicines in areas of unmet medical need. We endeavor to transform and simplify care for people with life-threatening illnesses around the world. Our portfolio of products and pipeline of investigational drugs includes treatments for HIV/AIDS, liver diseases, cancer, inflammatory and respiratory diseases, and cardiovascular conditions. Our portfolio of marketed products includes a number of category firsts, including complete treatment regimens for HIV infection available in a once-daily single pill, the first oral antiretroviral pill available to reduce the risk of acquiring HIV infection in certain high-risk adults, and the first Hepatitis C virus (HCV) treatment to provide a complete regimen in a single tablet. Gilead is committed to ensuring that people have access to our medicines.

While we appreciate the efforts of CMS to provide initial guidance regarding implementation of the MFP Program and to solicit stakeholder comments on portions of this guidance, Gilead is disappointed that CMS has only provided a thirty-day comment period, which is insufficient for stakeholders to provide robust feedback on guidance of this length and magnitude. This period falls far short of the sixty-day notice and comment period that the Department of Health and Human Services (HHS) provides “in most cases”²—including for programs, rules, regulations that are far less complex and with far fewer ramifications, and fails to

¹ Memorandum from Meena Seshamani, M.D., Ph.D., CMS Deputy Administrator and Director of the Center for Medicare to Interested Parties (March 15, 2023), <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

² See HHS How to Participate in the Rulemaking Process, <https://www.hhs.gov/sites/default/files/regulations/rulemaking-tool-kit.pdf>.

align with the principles set forth in HHS’s Good Guidance Practices Final Rule.³ We encourage CMS provide at least a sixty-day comment period for future guidance.

We are also concerned that CMS chose to issue Section 30 of the Initial Guidance “as final, without a comment solicitation.”⁴ Although CMS officials previously stated an intent to “engag[e] stakeholders . . . throughout [the IRA implementation] process,” the Agency has not provided an opportunity for the public to review and comment on Section 30.⁵ This lack of engagement of stakeholders is inconsistent with the Biden Administration’s Executive Order that “regulatory actions should be informed by input from interested or affected communities;...interested or affected parties in the private sector and other regulated entities; those with expertise in relevant disciplines; and the public as a whole.”⁶ The Executive Order also provides that agencies shall incorporate “best practices for information accessibility and engagement with interested or affected parties, including, as practicable and appropriate, community-based outreach; outreach to organizations that work with interested or affected parties;...and expansion of public capacity for engaging in the rulemaking process.”⁷ It is important that CMS solicit comments on all portions of the Initial Guidance through a public docket and respond in a revised guidance document, so that manufacturers and other stakeholders can have an opportunity to submit comments and review CMS responses to concerns raised.

The comments that follow are intended to further build on suggestions in the comments of our trade associations, the Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Innovation Organization (BIO). In particular, Gilead echoes our trade associations’ concern that the MFP Program could hinder continued biopharmaceutical innovation. As described further below, these risks are particularly acute with respect to HIV treatments and could hinder discovery of an eventual cure. We also urge CMS to implement the MFP Program in accordance with the statute, including enforcing the statutory limitation on duplicate discounts. Failing to enforce such limitations will exacerbate the impact of the IRA on the incentives and resources of manufacturers to invest in the development of innovative drugs and therefore further limit the scope of therapies patients will be able to access in the future.

Our specific recommendations can be summarized as follows:

- CMS Should Establish a Robust Process to Prevent MFP and 340B Duplicate Discounts. Gilead appreciates that manufacturers are allowed to provide access to the MFP through a retroactive reimbursement approach, which supports verification that a selected drug was dispensed to an MFP eligible individual and avoids duplicate MFP and 340B discounts on the same unit of dispensed drug. We encourage CMS to issue more detailed guidance regarding the retrospective reimbursement process. Such guidance should (1) clarify that manufacturers may use a retroactive reimbursement model to implement the 340B price, (2) require that pharmacies use a uniform, mandatory standard for reporting 340B units,

³ 85 Fed. Reg. 78770 (Dec. 7, 2020).

⁴ Initial Guidance § 30.

⁵ CMS National Stakeholder Call (Aug. 25, 2022), <https://www.cms.gov/files/document/transcriptnatoastakeholdercallonira08252022.pdf>.

⁶ Executive Order on Modernizing Regulatory Review, Exec. Order No. 14094, 88 Fed. Reg. 21879, 21879 (Apr. 6, 2023), <https://www.whitehouse.gov/briefing-room/presidential-actions/2023/04/06/executive-order-on-modernizing-regulatory-review/>.

⁷ *Id.* at 21880.

(3) implement a claims clearinghouse model to validate 340B claims, (4) establish a neutral third party administrator to administer retrospective MFP discounts while reconsidering use of Average Acquisition Cost in calculating those discounts, and (5) ensure that manufacturers are provided timely and accurate Prescription Drug Event (PDE) data with 340B identifiers.

- CMS Should Enter into Separate Medicare Drug Price Negotiation Agreements with Primary and Secondary Manufacturers. Requiring Primary Manufacturers to collect proprietary information from Secondary Manufacturers and making them responsible for ensuring that the Secondary Manufacturer provides MFP pricing is inappropriate, because it would raise business fairness and antitrust concerns and would be difficult to operationalize.
- CMS Should Provide Manufacturers Clarity on the Program Data Elements and Adequate Time to Collect Data. Gilead urges CMS to provide more clarity to manufacturers around the definitions of the MFP Program data elements and avoid discouraging manufacturers from offering discounted pricing to customers that Congress has consistently excluded from government pricing metrics. In addition, CMS should provide manufacturers with more than thirty (30) days to collect and report these numerous data elements.
- CMS Should Not Consider “Therapeutic Alternatives” for Purposes of Developing the MFP for HIV Medicines and Should Set the MFP for HIV Drugs Approved Under an NDA at the MFP Ceiling. Considering HIV medicines as therapeutic alternatives of one another for the purposes of developing the MFP fails to recognize how HIV therapies work, specifically that HIV drugs are unique, and each drug has specific qualities related to safety and tolerability, drug-drug interactions, dosing and drug resistance that should be considered when selecting the best HIV treatment regimen for a patient. Constructing therapeutic alternatives for HIV medicines for purposes of developing the MFP would also undermine progress on eliminating HIV and harm patients by disincentivizing innovation in treatment and cure development. To avoid disincentivizing the development of future HIV treatments and cures, CMS should set the MFP for HIV drugs approved under an NDA at the MFP ceiling to avoid disproportionately impacting investments in such drugs.
- CMS Should Define and Select Therapeutic Alternatives Based on Clinical Appropriateness. Gilead urges CMS to clarify that the selection of therapeutic alternatives should be based exclusively on clinical appropriateness, rather than cost of therapy. Clinical appropriateness should be determined through review of clinical guidelines, and through input from clinical experts, manufacturers, and providers. While we strongly believe there are no therapeutic alternatives for HIV treatments, if CMS uses comparators in the negotiation process for an HIV drug, CMS should rely on the HHS HIV guidelines. For example, a single tablet regimen with an A1 recommendation as an initial regimen for most people with HIV should only be compared to other single tablet regimens with “A1” recommendations for the same population. Multi tablet regimens are not appropriate comparators for single tablet regimens.

- CMS Should Broaden the Definition of Unmet Medical Need to Reduce Harm to Subpopulations with High Disease Burden. Gilead urges CMS to broaden the definition of the unmet medical need factor in Section 50.2 of the Initial Guidance to consider patient subpopulations within the disease that have high disease burden—such as specific and difficult forms of a disease—and unmet need. In those cases, a medicine may help to close disparities between populations. For example, people who inject drugs, lower income populations, and stigmatized populations are more likely to be infected with HIV but can also face greater challenges in adhering to medicines because of these same challenges.
- CMS Should Define Clearer Standards for Determining the MFP that Consider Societal Benefit, Transmission of Disease, and Public Health Impact When Measuring the Value of Selected Drugs. Gilead requests that CMS establish a more defined process for determining the MFP and clarify how data and evidence will be appraised and how such appraisal will impact the initially offered price. Specifically, Gilead urges CMS to (1) weight value-based factors much more heavily in determining the initial offer than cost-recovery factors (*e.g.*, R&D costs), (2) use a societal perspective and capture a broad range of outcomes and elements of value rather than focusing on a narrow, payer perspective of value, and (3) consider long-term impact rather than focusing on short-term or yearly impact that aligns with a government or payer’s budgetary cycles. Gilead also recommends that CMS avoid the use of cost effectiveness metrics, which can fail to reflect the diverse experience of the broad patient community by assuming uniform value across patient groups.

Our more detailed comments on the Initial Guidance are set forth below. We hope that CMS will consider these comments when developing further guidance.

I. Requirements for Manufacturers of Selected Drugs (Section 40)

A. CMS Should Establish a Robust Process to Prevent MFP and 340B Duplicate Discounts.

Gilead appreciates that the Initial Guidance would allow manufacturers to provide access to the MFP by “providing retrospective reimbursement for the difference between the dispensing entity’s acquisition cost and the MFP.”⁸ We believe a retroactive reimbursement approach is critical to (1) enabling verification that a selected drug was in fact dispensed to a MFP-eligible individual, and (2) avoiding duplicate MFP and 340B discounts on the same unit of product. As CMS acknowledges, and as required by the IRA, manufacturers of selected drugs are only required to provide the lower of the MFP *or* the 340B ceiling price—but not both—when a covered entity dispenses a selected drug to a Medicare beneficiary that is a “patient” of the covered entity.⁹ Without more detailed guidance, however, it will be difficult for CMS and manufacturers to prevent diversion of drugs sold at the MFP price and identify and prevent duplicate discount in accordance with the IRA.

⁸ Initial Guidance § 40.4.

⁹ SSA § 1193(d); Initial Guidance § 40.4.1.

i. HHS Should Clarify that Manufacturers May Also Use a Retrospective Reimbursement Model to Implement the 340B Ceiling Price

In the course of implementing the IRA, HHS is presented with an opportunity to align the MFP Program and the 340B Program through use of the retrospective reimbursement model for both programs. The Initial Guidance provides that “[i]f the 340B ceiling price is subsequently determined to be lower than the MFP, then the manufacturer would be responsible for providing to the covered entity the difference between the MFP and the 340B ceiling price.”¹⁰ This statement seems to contemplate that manufacturers would provide access to the MFP to covered entities *before* the 340B discount is provided. Under the current discount model used by covered entities, however, the 340B discount is provided upfront, rather than through a back-end rebate. We believe that a retrospective rebate model could also promote the integrity of the 340B program, and we support the use of such model as contemplated in the Initial Guidance. We thus encourage CMS to work with the Health Resources and Services Administration (HRSA) to clarify that manufacturers may also use a retrospective reimbursement model to implement the 340B ceiling price. This approach would simplify the process for identifying duplicate MFP and 340B discounts, while leveraging the opportunity to improve, strengthen, and streamline the 340B Program.

ii. To Ensure an Accurate and Timely PDE Record, CMS Should Require that Pharmacies Use, a Uniform, Mandatory Standard for Reporting 340B Units

Gilead supports the 340B Program as one way to ensure broader access to medicines for uninsured, low-income patients. We are concerned, however, based in part on our experience with the 340B Program, that unless further guidance is provided and sufficient guardrails are put in place, it will be difficult, if not impossible, to identify and prevent duplicate discounts consistent with the IRA. The 340B program has experienced unprecedented growth in recent years; by one estimate, purchases under the 340B Program totaled more than \$40 billion in 2021, an increase of 15.6% over 2020.¹¹ Gilead has developed robust processes and procedures to identify rebate claims by state Medicaid programs for drugs purchased by covered entities through the 340B Program.¹² Yet, despite our efforts, these processes have inherent limitations, due to, in large part, to limited quality and availability of Medicaid claims-level data and lack of agency guidance for preventing duplicate discounts. The biggest barrier to Gilead identifying and preventing duplicate discount is lack of sufficient data, both with respect to the availability of claims-level data and the quality of the data that is available. CMS will need to issue further guidance that establishes a mechanism for the provision of claims level data, or we will continue to have challenges identifying and preventing duplicate discounts as we implement the MFP Program.

It is thus critically important that CMS establish a uniform, mandatory standard for reporting 340B units on the PDE record. Covered entities currently do not consistently include 340B modifiers on insurance claims, particularly if use of such modifiers is not mandatory. A recent study found that “[m]odifier usage reached 90% in some segments when reporting was mandatory, fell below 20% when it was optional, and dropped below 1% when it was

¹⁰ Initial Guidance § 40.4.1.

¹¹ Drug Channels, *The 340B Program Climbed to \$44 Billion in 2021—With Hospitals Grabbing Most of the Money* (Aug. 15, 2022), <https://www.drugchannels.net/2022/08/the-340b-program-climbed-to-44-billion.html>.

¹² See 42 U.S.C. § 256b(a)(5)(A).

impractical.”¹³ Unless CMS establishes a uniform, mandatory standard for reporting 340B units, 340B modifiers will not be used consistently, thwarting manufacturer efforts to comply with the statutory prohibition against duplicate MFP and 340B discounts.

Notably, 340B claims modifier usage was higher when the 340B status of the claim was known prior to or at the point-of-sale.¹⁴ Currently, however, it is less common for covered entities (and in particular, their contract pharmacies) to use a pre-purchased inventory model, where product pre-purchased at the 340B price is kept on the pharmacy shelf to fill the prescriptions for the covered entity’s patients. Instead, under the replenishment model, when filling a prescription, the contract pharmacy initially dispenses product purchased at a non-340B price. The pharmacy sends an electronic record of its claim to a third-party administrator (TPA), which reviews the claims to determine which prescriptions were filled by an eligible patient of the covered entity. Once the TPA has made its determinations, it transmits that information back to the pharmacy. After the contract pharmacy has dispensed a certain volume of a given drug to 340B-eligible patients, that volume is “replenished” with product purchased at the 340B price. Because a pharmacy using the replenishment model does not know the 340B status at the point of sale, the replenishment model poses significant challenges to the consistent use of a 340B indicator.¹⁵

Gilead recommends that CMS work with HRSA to require that all covered entities and contract pharmacies identify a patient as 340B-eligible at the point of sale and dispense product purchased under the 340B program to that patient. This identification requirement would help ensure that a pharmacy knows the 340B status of a particular unit of drug at the time the product is dispensed and thus can include a 340B indicator as appropriate on the claim, resulting in accurate claims information submitted in real time and prior to adjudication. Such a requirement should also apply regardless of the insurance that the patient presents at the time of dispense, since pharmacies may not be able to accurately determine whether the patient has Medicare Part D coverage at the point of sale. With respect to Medicare Part D claims, CMS also should require pharmacies to populate 340B identifier on the claim at the point of sale to identify the claim as either 340B or not 340B and require Part D plan sponsors to deny claims that do not have the field populated with one of these values.

iii. Additional Safeguards, Such as a 340B Claims Clearinghouse, are Needed if 340B Units are Identified After an Insurance Claim is Submitted

Although requiring a 340B identifier on each claim at the point of sale would be a timely and efficient way to ensure accurate PDE data, if HHS nevertheless permits covered entities and

¹³ Rory Martin, *et al.*, Can 340B Modifiers Avoid Duplicate Discounts in the IRA?, IQVIA White Paper (Feb. 2023), <https://www.iqvia.com/locations/united-states/library/white-papers/can-340b-modifiers-avoid-duplicate-discounts-in-the-ira10>.

¹⁴ *Id.* (The “340B status of a drug must be known at the point of sale to the patient in order to apply the modifier to the claim prior to adjudication. While this is possible for pharmacies that identify 340B transactions at the point of sale, which may occur in entity-owned pharmacies and often in those that use physical inventory, the drug’s 340B status is unknown for pharmacies using the 340B replenishment model and virtual inventory which is used by almost all contract pharmacies.”).

¹⁵ The HHS Office of Inspector General also has found that the replenishment model creates complications in preventing diversion and duplicate discounting under the 340B program. *See* OIG, Memorandum Report: Contract Pharmacy Arrangements in the 340B Program, OEI-05-13-00431 (Feb. 4, 2014), <https://oig.hhs.gov/oei/reports/oei-05-13-00431.pdf>.

their contract pharmacies to identify product as 340B-eligible after the product is dispensed (which can result in identification of the patient as 340B-eligible *after* the insurance claim is submitted), it is critical that HHS establish robust guardrails around the replenishment model to enable the accurate submission of 340B indicators.

First, HHS should limit the timeframe for replenishment, so that covered entities must determine whether a particular unit of product is subject to a 340B discount within a specified period after the product is dispensed. This timeframe should be shorter than the time period in which manufacturers are invoiced for MFP claims, so that units are identified as subject to a 340B discount *before* an MFP discount is requested on the same unit. Without such a limitation, it will be difficult, if not impossible, to determine in a timely manner if a claim is subject to duplicate discounts.

Second, if a covered entity identifies a product as subject to a 340B discount after the claim has been submitted, HHS (through CMS and HRSA) should establish a clear and straightforward process for the covered entity to timely identify such 340B claims. One option would be to create a 340B claims clearinghouse to promote the integrity of the 340B PDE indicator data. HHS could refer to the Oregon Medicaid program's model as an example of a claims clearinghouse that generally works effectively for this purpose today.¹⁶ Under this model, covered entities (and any 340B vendors or contract pharmacies that submit claims on their behalf) must identify and submit 340B claims for each calendar quarter to the clearinghouse within thirty days after the end of that quarter, and the state rebate vendor uses the 340B claims files to match up the original paid encounter and exclude the claim from the quarterly drug rebate process.¹⁷ If there is an error and a validation fails, it is sent back to the trading partner for correction.¹⁸ The Oregon model could be adapted to apply to MFP claims instead of Medicaid claims (recognizing that HHS would need to update the claims level data collected by the clearinghouse to include data applicable to the Medicare Part D program. The specific claims level data that should be required are described below). The claims data could be used to validate and update as needed the information provided on the MFP invoice. In addition, if a manufacturer reviews the claims data and identifies a unit that was not correctly identified as subject to a 340B discount, and the covered entity agrees that the claim should have been billed as a 340B claim, that manufacturer should have the ability to submit this information to the clearinghouse, including appropriate documentation of the covered entity's agreement, and the clearinghouse should update the claim information to reflect the 340B status. This will help increase the accuracy and integrity of the clearinghouse model.

If HHS implements a clearinghouse model, Gilead encourages HHS to clearly set forth applicable claims submission requirements for all 340B stakeholders. HHS should also establish penalties for covered entities that do not submit claims data to the clearinghouse in the specified period. For example, a covered entity's repeated failure to comply could result in losing eligibility for participating in Medicare Part D or the 340B program. Additionally, Gilead encourages HHS to employ the same clearinghouse to comply with other statutory requirements that involve

¹⁶ Oregon Health Authority, Retroactive 340B Claims File Instructions, <https://www.oregon.gov/oha/HSD/OHP/Tools/340B%20Claims%20File%20Instructions%20and%20Design.pdf>.

¹⁷ *Id.*

¹⁸ *Id.*

identifying 340B claims, such as the prohibition against Medicaid duplicate discounts¹⁹ and the non-duplication provision for Part D inflation-based rebates.²⁰

iv. CMS Should Use a Third-Party Administrator to Administer Retrospective MFP Discounts and Reconsider Use of Average Acquisition Cost in Calculating those Discounts

Gilead supports the use of a neutral, single third-party administrator (TPA) to administer retrospective MFP discounts across manufacturers, for the reasons described in the comment letters of our trade associations. Use of a TPA will allow for consistent patient access to the MFP at the point-of-sale, while also ensuring reimbursement to pharmacies through a standardized, central process with timely data. Moreover, using the same TPA to administer both the MFP discount program and the 340B clearinghouse would provide efficiencies, because the TPA could obtain Medicare Part D PDE data from CMS in addition to 340B claims information from covered entities, and use this information to remove 340B claims from the MFP invoices provided to manufacturers (unless the MFP is lower than the 340B ceiling price, in which case amount invoiced to the manufacturer would be reduced to equal the difference between the MFP and the 340B ceiling price).

We also ask CMS to reconsider use of the dispensing entity's actual acquisition cost (AAC) as the metric used to calculate MFP-based rebates. As discussed in PhRMA's comments regarding the Initial Guidance, AAC is hard to track and is not currently reported by pharmacies to other stakeholders. Using it may incentivize higher AACs in order to increase MFP rebates. Reporting AAC could also create misaligned incentives in contracting between pharmacies and other entities in the pharmaceutical supply chain. For example, if pharmacies report the AAC as part of the claim transaction between the pharmacy and Part D plan (or a PBM), knowledge of the AAC could allow the plan or PBM to undercut the pharmacy in negotiations for total pharmacy reimbursement.

v. Under Any Approach, CMS Must Ensure that Manufacturers Have Timely and Accurate PDE Data with 340B Identifiers

Finally, regardless of whether CMS chooses to utilize a claims clearinghouse model and/or a TPA, CMS (directly or through the TPA) should provide manufacturers with PDE data, including 340B identifiers, to enable identification of MFP-eligible claims and prevent diversion of product subject to the MFP discount to individuals that are not MFP-eligible individuals. It is critical that manufacturers receive accurate and timely PDE data to ensure to integrity of the Program. Such claims data should, at a minimum, include the following data fields:

- Part D Contract ID and Part D Plan Benefit Package ID
- Prescription Number
- Rx BIN Number
- Prescribed Date
- Fill Date (i.e., date of service)
- 9-digit National Drug Code (NDC)

¹⁹ Public Health Service Act § 340B(a)(5)(A).

²⁰ SSA § 1860D-14B(b)(1)(B).

- Standardized Numerical Identification (SNI)
- Quantity dispensed
- Pharmacy ID
- Prescriber ID
- Wholesaler Invoice Number
- 340B Covered Entity ID/NPI
- 340B claims identifier

Without access to the foregoing data in a timely manner, it will not be possible for manufacturers to appropriately identify and eliminate units that may otherwise be subject to duplicate MFP and 340B discounts.

We note that the collection and aggregation of the foregoing data fields should not present any concerns with respect to protected health information, as manufacturers can be provided with these data fields for purposes of validating rebate claims.²¹ Manufacturers' access to the same information from the PDE data is necessary to ensuring appropriate identification of MFP-eligible claims and preventing the diversion of product subject to the MFP discount to individuals that are not MFP-eligible.

vi. Manufacturers Must Have Adequate Time to Review the PDE Data Prior to Providing Retroactive Reimbursement of MFE

Lastly, CMS should measure the time period in which manufacturers must provide access to the MFP to reimburse pharmacies from the date on which the manufacturer receives all data necessary to validate the eligibility of the underlying MFP rebate claim, rather than the date the product is dispensed to the patient. Given that plans submit PDE entries to CMS on a two-week cycle,²² the necessary claims level data elements described above may not even be available within

²¹ HHS, Does the Privacy Rule Permit State Medicaid Agencies to Disclose Protected Health Information to Pharmaceutical Manufacturers and Third Party Data Vendors for Purposes of Validating Claims under the Medicaid Drug Rebate Program?, <https://www.hhs.gov/hipaa/for-professionals/faq/456/does-hipaa-permit-state-medicaid-agencies-to-disclose-information-to-pharmaceutical-manufacturers/index.html> (“The Privacy Rule permits State Medicaid agencies to disclose protected health information, such as prescription numbers, to pharmaceutical manufacturers and third party data vendors that assist the pharmaceutical manufacturers, for purposes of validating claims submitted under the Medicaid Drug Rebate program. Because the amount of the rebate is based on drug utilization by individual enrollees, such disclosures are permitted as part of a State Medicaid agency’s payment activities.”); HHS, Does the Privacy Rule Permit Health Plans to Disclose Protected Health Information to Pharmaceutical Manufacturers for the Adjudication of Drug Rebate Contracts?, <https://www.hhs.gov/hipaa/for-professionals/faq/455/does-hipaa-permit-health-plans-to-disclose-information-to-pharmaceutical-manufacturers/index.html> (“The Privacy Rule permits a health plan to disclose protected health information, such as prescription numbers, to a pharmaceutical manufacturer for purposes of adjudicating claims submitted under a drug rebate contract. Because the amount of the rebate is based on drug utilization by individual enrollees, such disclosures are permitted as part of a covered entity’s payment activities.”). Medicare is considered a “health plan” for HIPAA Privacy Rule purposes. 45 CFR § 160.103 (including, under the definition of “Health Plan,” Parts A, B, and C of the Medicare program and an issuer of a Medicare supplemental policy).

²² See Contract Year (CY) 2022 Part D Pricing Data Submission Guidance, CMS (May 28, 2021), <https://www.cms.gov/files/document/cy2022drugpricingsubmissionguidelines05282021final.pdf>.

14 days of the date the product is dispensed to the patient—rendering a manufacturer unable to determine if a unit is subject to duplicate discounts.

In addition, even once the manufacturer receives the necessary data, validating claims with 14 days is not feasible. Other government rebate programs provide manufacturers a much longer period in which to pay claims. For example, manufacturers have 38-days after receiving an invoice to pay a discount under the Part D Coverage Gap Discount Program,²³ and 37-days to pay a rebate after receiving a rebate invoice under the Medicaid Drug Rebate Program (MDRP).²⁴ Given the “novel” and “complex” nature of the MFP Program,²⁵ Gilead urges CMS to provide manufacturers at least this long to review and validate MFP discount claims before the manufacturer is required to pay such claims.

B. CMS Should Enter into Separate Medicare Drug Price Negotiation Agreements with Primary and Secondary Manufacturers

Section 40 of the Initial Guidance provides that if “more than one entity meets the statutory definition of manufacturer for a selected drug,” CMS “intends to designate the entity that holds the NDA(s)/BLA(s) for the selected drug to be ‘the manufacturer’ of the selected drug (hereinafter ‘Primary Manufacturer’).” Any other entity that meets the statutory definition of manufacturer for a drug product included in the selected drug and “either (1) is listed as a manufacturer in an NDA or BLA for the selected drug or (2) markets the selected drug pursuant to an agreement with the Primary Manufacturer” would be a “Secondary Manufacturer.” Secondary Manufacturers would include any manufacturer of any authorized generics and any repackager or relabeler of the selected drug that “meet these criteria.” CMS intends to sign an agreement only with the Primary Manufacturer, and the Primary Manufacturer would be required to, among other things: (1) report manufacturer-specific information for the Secondary Manufacturer (in some cases blending that information with the Primary Manufacturer's own data to report combined pricing metrics); (2) ensure that the Secondary Manufacturer make the MFP available to MFP-eligible individuals; and (3) pay civil monetary penalties (CMPs) for violations stemming from noncompliance by any Secondary Manufacturer.

Gilead has significant concerns with CMS’ proposal. As a threshold matter, the IRA does not authorize CMS to impose program requirements or penalties on a distinct corporate entity, which is the effect of the Primary/Secondary Manufacturer policy. In addition, the Initial Guidance would require Primary Manufacturers to have insight into and control over aspects of the Secondary Manufacturer’s pricing, particularly where the Primary Manufacturer and Secondary Manufacturer are not affiliates. Reporting the required data under Section 40.2, Section 50.1, and Appendix C of the Initial Guidance to CMS would require Primary Manufacturers to access proprietary information from Secondary Manufacturers, who may be competitors, raising both business fairness concerns and legal antitrust issues. Moreover, a process of obtaining this information from Secondary Manufacturers is not feasible for the Primary Manufacturer to operationalize.

²³ 42 C.F.R. § 423.2315(b)(3).

²⁴ Interest Calculation for Late Rebate Payments, CMS, <https://www.medicaid.gov/medicaid/prescription-drugs/medicaid-drug-rebate-program/interest-calculation-for-late-rebate-payments/index.html>.

²⁵ 87 Fed. Reg. 62433, 62433 (Oct. 14, 2022).

For these reasons, Gilead recommends that CMS not adopt the Initial Guidance on Primary and Secondary Manufacturers as final. Instead, CMS should adopt an approach similar to the one it uses in the MDRP. Under the MDRP, CMS enters into separate National Drug Rebate Agreements with each labeler and holds each labeler individually responsible for compliance with the requirements of that agreement. Likewise, if more than one distinct legal corporate entity meets the definition of manufacturer under the IRA, CMS should enter into separate agreements with each manufacturer. This approach is consistent with the text and structure of the IRA, which adopts the definition of “manufacturer” in Social Security Act § 1847A(c)(6)(A), which in turn cross-references the definition of “manufacturer” in the Medicaid rebate statute.²⁶ In addition, the IRA contemplates multiple agreements with multiple manufacturers, stating that the “Secretary shall enter into agreements with manufacturers of selected drugs.”²⁷ Entering into separate agreements with each Primary and Second Manufacturer also avoids discouraging manufacturers from entering into arrangements with authorized generic manufacturers, repackagers, and relabelers. Such arrangements are pro-competitive and consistent with Congress’ goals of lowering drug prices.

C. CMS Should Support Accurate Submission of Data by Providing Manufacturers Clarity on the Data Elements and Adequate Time to Collect Data

Gilead recognizes that CMS has issued a separate information collection request (ICR) regarding the MFP Program data elements that would be required to be reported for initial price applicability year 2026.²⁸ We note at a high level, however, that it is particularly important that CMS provide additional clarity to manufacturers around the definitions of these data elements and, in doing so, avoid discouraging manufacturers from offering discounted pricing to customers that Congress has consistently excluded from government pricing metrics. In particular, many of the market data, revenue, and sales volume data elements included in Appendix C of the Initial Guidance are new and reference terms such as “commercial” prices are not defined. In the context of the MDRP and the Medicare Average Sales Price (ASP) program, Congress has specifically excluded “any prices” to certain customers, such as the Department of Veterans Affairs (VA) and 340B covered entities, from the pricing metrics under those programs, so that manufacturers can offer discounted pricing to those customers without impacting their prices to the entire Medicare and Medicaid programs. CMS should take a similar approach here and clarify that “commercial” prices exclude prices to ASP and Best Price-exempt customers.

In addition, CMS should provide manufacturers with more than thirty (30) days to collect and report these numerous data elements. Manufacturers generally have at least a quarter to calculate pricing metrics reported to government healthcare programs, such as Best Price and ASP, and they have forty-five days to calculate Non-FAMP, which is the pricing metric specifically identified in Section 11001 of the IRA. CMS should provide manufacturers at least this much time to report the data elements identified in Section 40.2, Section 50.1, and Appendix C of the Initial Guidance, which are more numerous than those required under other government healthcare programs and in many cases are completely new. This will help support accurate and complete manufacturer submissions and thus further the integrity of the MFP Program. We also encourage

²⁶ SSA § 1191(c)(1) (referencing SSA § 1847A(c)(6)(A), referencing SSA § 1927(k)(5)).

²⁷ SSA § 1193(a) (emphasis added).

²⁸ 88 Fed. Reg. 16983 (Mar. 21, 2023).

CMS to provide an opportunity for manufacturers to submit additional information to address questions or misunderstandings regarding their data submissions.

II. Negotiation Factors and Negotiation Process (Sections 50 and 60)

Gilead is concerned that CMS’ framework for setting MFPs has the potential to disincentivize innovation in important therapeutic areas, such as HIV. By significantly shortening the effective time period in which a manufacturer can determine its own price for a product in the Medicare market, the IRA has the potential to undermine the incentives created by the patent system. Any limitation to these incentives can have a negative result for innovation and ultimately patients. This could lead to less investment and could result in fewer new drugs for unmet medical needs.

This impact is particularly concerning for HIV medicines. As manufacturers develop novel HIV therapies, these innovations over time form important building blocks toward a cure for HIV. If CMS’ negotiation process disincentivizes innovation in the HIV therapeutic area, this will stifle the incremental innovation that Gilead believes is critical to ending the HIV epidemic and which are building toward an eventual cure for HIV. As described further below, CMS should clarify that HIV medicines do not have therapeutic alternatives for purposes of determining the MFP. In addition, we urge CMS to define clearer standards for the methodology and process for measuring the value of selected drugs and determining the MFP, and to consider the societal benefit of the drug and public health impacts such as transmission of disease.

A. CMS Should Not Consider HIV Medicines “Therapeutic Alternatives” for Purposes of Developing the MFP and Should Set the MFP for HIV Drugs Approved Under an NDA at the MFP Ceiling

Gilead strongly disagrees with CMS’ proposal to set the “starting point price” for the initial offer based on the Part D net prices and/or ASPs of therapeutic alternatives, as this overlooks the unique needs of patients and could result in unfairly low prices. As described further below, the use of therapeutic reference pricing—both in development of the starting point price and subsequent adjustments to that price—is particularly inappropriate for HIV medicines. Gilead therefore urges CMS to consider HIV selected drugs to have no therapeutic alternatives during the initial offer or counteroffer process.

Considering HIV medicines as therapeutic alternatives of one another for purposes of developing the MFP fails to recognize that HIV drugs are unique, and each drug has specific qualities related to safety and tolerability, drug-drug interactions, dosing and drug resistance that should be considered when selecting the best HIV treatment regimen for a patient. Assuming treatments are therapeutic equivalents would not recognize the significant public health value that the full scope of HIV treatments provides for patients. Prescribers must consider the patient’s specific drug resistance, co-morbidities, and the impact of side effects when making a prescribing decision for each patient. Early treatment initiation with the right antiretroviral product for the

patient is critical to achieving better individual patient health outcomes, as well as significantly decreasing the risk of HIV transmission to others.²⁹

A provider's careful selection of a treatment regimen supports patient medication adherence and increases each patient's chance of achieving and sustaining viral suppression.³⁰ Viral suppression stops HIV infection from progressing, helping people living with HIV stay healthy and live longer, while effectively eliminating risk of sexually transmitting the virus to an HIV-negative partner.³¹ A 2018 study found that 86% of people living with HIV have been diagnosed by a healthcare provider, but only 60% of the diagnosed population has achieved viral suppression. Of the diagnosed population, only 57% receive ongoing care.³² Even among those patients who continue to receive treatment, many have experienced and struggled with treatment adherence.

Finding the right individual treatment to promote patient adherence and persistence is crucial to ending the HIV epidemic: a recent report states that if an Incidence : Prevalence ratio of less than 0.03 is maintained over time, the epidemic would be eliminated.³³ This report found that “viral suppression on reducing incidence will only be fully realized when testing and treatment targets are achieved in all populations.”³⁴ This underscores the significant need for better and broader optionality in treatment choice, enabling clinicians to tailor regimens to different patient populations with the aim of improving not only adherence but also persistence and therefore clinical outcomes. Continued innovation in the HIV therapeutic area can help address those challenges while work continues toward development of an eventual cure.

Use of therapeutic reference pricing will undermine progress on eliminating HIV and harm patients by disincentivizing manufacturers to develop novel HIV treatments, especially those designed to reach people who experience system inequities and disparities in accessing healthcare. Innovation in HIV treatment is ongoing to provide patients with more options to meet their clinical needs and preferences and achieve sustained viral suppression. Treating these medicines as therapeutic equivalents of each other devalues these benefits, to the detriment of HIV patients. Advancements in HIV treatments have resulted in regimens that are highly effective, have high barriers to drug resistance, and have unsurpassed tolerability and safety. The advances in HIV medicine means that certain HIV regimens can be started immediately after HIV diagnosis—also

²⁹ Lodi S., Phillips A., Logan R., et al., Comparative effectiveness of immediate antiretroviral therapy versus CD4-based initiation in HIV-positive individuals in high-income countries: observational cohort study, 2 LANCET HIV E335-43 (2015).

³⁰ NIH, HIV Treatment, <https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-treatment-adherence> (explaining that “[t]aking HIV medicines every day prevents HIV from multiplying, which reduces the risk that HIV will mutate and produce drug-resistant HIV.”); see also *Ending the HIV Epidemic in the U.S.*, CDC, <https://www.cdc.gov/endhiv/treat.html> (noting that treating people with HIV “rapidly and effectively” will help “reach sustained viral suppression.”).

³¹ See National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases, 10 Things to know about HIV Suppression (November 14, 2017), <https://www.niaid.nih.gov/news-events/10-things-knowabout-hiv-suppression>.

³² CDC, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention, Division of HIV/AIDS Prevention, Understanding the HIV Care Continuum, figs. 1 & 2 (2018), <https://www.cdc.gov/hiv/pdf/library/factsheets/cdc-hiv-care-continuum.pdf>.

³³ Frescura L, Godfrey-Faussett P, Feizzadeh A, El-Sadr W, Syarif O, Ghys PD; on and behalf of the 2025 testing treatment target Working Group. Achieving the 95 95 95 targets for all: A pathway to ending AIDS. PLoS One. 2022 Aug 4;17(8):e0272405. doi: 10.1371/journal.pone.0272405. PMID: 35925943; PMCID: PMC9352102.

³⁴ *Id.*

known as rapid start of HIV treatment—before results of recommended resistance testing or baseline laboratory testing are available.³⁵ Certain modern HIV regimens support innovative models of care like telehealth and telemedicine services for HIV treatment and prevention because they require less clinical monitoring.³⁶ The ongoing development of long-acting HIV medicines also is an important step towards supporting adherence for patients living with or at risk for HIV and offers new treatment options to patients who may not be well-suited to taking a daily oral pill. These newer daily oral single tablet regimens and long-acting medicines have potential to improve adherence for patients who live in difficult circumstances where taking a daily pill is impossible, and would provide an option for individuals with multi-drug resistant forms of HIV.³⁷ In addition, treatments that can be administered less frequently than daily dosing could provide options for those who find daily dosing challenging, with the aim of improving not only adherence but also persistence and therefore better clinical outcomes. Treating these medicines as therapeutically equivalent to older medicines would undermine innovation by ignoring the value of these treatments to patients and the healthcare system and undervaluing or disregarding entirely research and development costs.

There is longstanding recognition in the Medicare program that patients need access to the particular HIV medication that was prescribed for them, and that one HIV product cannot simply stand in for another. As CMS itself has previously recognized in the context of the Medicare Part D protected classes policy, with respect to antiretrovirals, there are a “number of multiple drug combinations and adjunctive therapies involved,” drug protocols are subject to change, and changing drug resistance plays a role “in determining the selection of among the different antiretroviral drugs.”³⁸ Moreover, CMS has acknowledged that “[t]he need to adjust specific combination antiretroviral therapy in real time is complex and must consider, among other things, viral sensitivity to the drugs, drug interactions, pregnancy status (if applicable), and potentially the patient’s pharmacogenomic profile of the cytochrome P450 system.”³⁹ HHS’ guidelines on HIV treatment also state that “selection of a regimen should be individualized” to the patient based on factors such as virologic efficacy, potential adverse effects, pill burden, drug–drug interaction potential, and comorbid conditions.⁴⁰ CMS should align with this recognition that no one treatment

³⁵ See, e.g., AIDS Education & Training Center Program, Rapid ART, <https://aidsetc.org/sites/default/files/media/document/2023-03/ncrc-rapidart-1-pager.pdf> (providing that Rapid (or immediate) ART can be appropriate for people with suspected acute HIV infection, with or without a confirmed HIV diagnosis).

³⁶ See, e.g., CDC, Telehealth for HIV Prevention and Care Services, <https://www.cdc.gov/hiv/effective-interventions/treat/telehealth/index.html> (stating that “[t]elehealth can be leveraged to increase access to HIV prevention and care services, to improve their acceptability, and to close these gaps. Telehealth can be used as a strategy to support early HIV diagnosis and initiation of treatment, sustained viral suppression, prevention of new HIV transmissions, and rapid response to HIV outbreaks.”).

³⁷ See, e.g., Gilead Sciences, Inc., Long-Acting Lenacapavir in People with Multidrug-Resistant HIV-1: Week 52 Results, https://www.croiconference.org/wp-content/uploads/sites/2/posters/2022/CROI2022_Poster_491.pdf (demonstrating that long-acting Lenacapavir could reduce the daily pill burden for HIV patients).

³⁸ Medicare Program; Contract Year 2015 Policy and Technical Changes to the Medicare Advantage and the Medicare Prescription Drug Benefit Programs; Proposed Rule, 79 Fed. Reg. 1918, 1944 (Jan. 10, 2014).

³⁹ *Id.*

⁴⁰ HHS, Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV, G-4 (Mar. 23, 2023), <https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv>.

HIV regimen has a clear therapeutic alternative and clarify that HIV medications do not have therapeutic alternatives for purposes of determining the MFP.

We also note that while drugs approved under a New Drug Application (NDA) are potentially subject to negotiation after only *seven* years, biological products approved under a Biologics License Application (BLA) are not subject to negotiation for *eleven* years.⁴¹ HIV treatments generally are approved under NDAs and therefore subject to the MFP Program four years sooner than would be a comparable biological product. This distinction does not reflect the value that HIV medicines bring to patients and to the public health at large. To avoid disincentivizing the development of HIV treatments arbitrarily simply because of their approval pathway, CMS should set the MFP for HIV drugs approved under an NDA at the MFP ceiling to avoid disproportionately impacting investments in such drugs.

B. CMS Should Define and Select Therapeutic Alternatives Based on Clinical Appropriateness

Gilead urges CMS to clarify that the selection of therapeutic alternatives should be based exclusively on clinical appropriateness, rather than cost of therapy. The statute’s reference to “therapeutic” alternatives makes clear that such alternatives should be selected based on their therapeutic use.⁴² Clinical appropriateness should be determined through review of clinical guidelines, input from clinical experts, manufacturers, and providers, and other related methods. We emphasize that manufacturers and healthcare providers have particularly deep knowledge and experience regarding selected drugs, and thus it is crucial that CMS meaningfully engage with these stakeholders when determining therapeutic alternatives. While we strongly believe there are no therapeutic alternatives for HIV treatments, if CMS uses comparators in the negotiation process for an HIV drug, CMS should rely on the HHS HIV guidelines. For example, a single tablet regimen with an “A1” recommendation as an initial regimen for most people with HIV should only be compared to other single tablet regimens with “A1” recommendations for the same population.⁴³ Multi tablet regimens are not appropriate comparators for single tablet regimens.

C. CMS Should Broaden the Definition of Unmet Medical Need to Reduce Harm to Subpopulations with High Disease Burden

Unmet medical need is defined narrowly in Section 50.2 and Section 60.3.3.1 of the Initial Guidance, focusing on diseases for which there are very limited or no treatment options. This definition should be broadened to consider patient subpopulations within the disease that have high disease burden—such as specific and difficult forms of a disease—and unmet need. In those cases, a medicine may help to close disparities between populations. For example, people who inject drugs, lower income populations, and stigmatized populations are more likely to be infected with HIV but can also face greater challenges in adhering to medicines because of these same challenges. Patients who do not adhere to existing HIV treatments may become resistant to such

⁴¹ See SSA § 1192(e)(1)(A)(ii), (B)(ii).

⁴² Only then, *after* the therapeutic alternatives are identified, can CMS consider their costs as a factor in determining the MFP. SSA § 1194(e)(2).

⁴³ HHS, Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. What to Start: Initial Combination Antiretroviral Regimens for People with HIV. (Sep. 21, 2022). <https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/what-start-initial-combination-regimens?view=full>.

medicines and need new options to treat their disease. Resistance may also develop over time in highly treatment experienced (HTE) patients, leading to high disease burden and few choices for effective therapies. As discussed above, there is a significant need for better and broader optionality in treatment choice, allowing healthcare providers to tailor regimens to patients with the aim of improving not only adherence but also persistence and therefore clinical outcomes. If CMS does not consider the need for continued innovation in a therapeutic area such as HIV, it risks decimating future research and investment in that therapeutic area, to the particular detriment of patients experiencing disparities and inequities in the U.S. healthcare system.

We also note that the definition of “unmet medical need” in the Initial Guidance is much narrower than the definition the FDA uses. FDA defines unmet medical need as “a condition whose treatment or diagnosis is not addressed adequately by available therapy” that includes either “an immediate need for a defined population” or “a longer-term need for society.”⁴⁴ FDA further explains that such a drug will treat a condition (1) where there is no available therapy; (2) where there is available therapy, but the drug presents additional benefits; and (3) where the only available therapy was approved under the accelerated approval program and clinical benefit against the primary endpoint has not yet been verified.⁴⁵ Broadening the definition of unmet medical need to consider patient subpopulations within the disease that have high disease burden would better align with this existing agency guidance.

D. CMS Should Define Clearer Standards for Determining the MFP that Consider Societal Benefit, Transmission of Disease, and Public Health Impact When Measuring the Value of Selected Drugs

Gilead appreciates CMS’ intention to avoid establishing an overly rigid, formulaic process for determining the MFP. Such a process likely would not include the necessary flexibility to fully capture the value of different types of therapies. The process and methodology outlined in the Initial Guidance, however, is too unstructured and open-ended to satisfy the statutory requirement that CMS implement a “consistent methodology and process” for setting MFPs.⁴⁶ We are concerned that CMS’ proposed methodology and process are unclear and could be applied inconsistently, which will result in prices that are arbitrary and are certainly not fair to the manufacturer.

Accordingly, we request that CMS establish a more defined process to improve predictability, while still retaining flexibility to account for differences in value across therapies. We encourage CMS to define a specific approach that is clearer as to how data and evidence will be appraised, and how that appraisal will impact (or be weighted compared to other factors) the offered price. As part of that process, we recommend that:

- Value-based factors (*e.g.*, comparative effectiveness and unmet need) should be weighted much more heavily in determining the initial offer than cost-recovery factors (*e.g.*, R&D costs). This will help incentivize innovation by focusing on the value of treatment to individual patients and the greater society, rather than limiting innovation by focusing on development costs.

⁴⁴ FDA, Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics (2014), <https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf>

⁴⁵ *Id.*

⁴⁶ SSA § 1194.

- CMS should use a societal perspective and capture a broad range of outcomes and elements of value rather than focusing on a payer perspective of value which focuses on a narrow set of clinical outcomes. This is recognized as a best practice by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and the health economics community. This includes consideration of value measures such as adherence, productivity, disease severity, impact on total cost of care, limiting transmission of infectious diseases, and scientific spillover/innovation.⁴⁷
- For any type of outcome or evidence-based measure used, it is critical that CMS consider long-term impact rather than focusing on short-term or yearly impact that aligns with budgetary cycles. Health economic analysis typically would not show cost offsets in a single year. If CMS focuses on short-term or yearly impact, it will lack the ability to account for the product's full public health impact and/or cost-saving potential that accrues over time.

Gilead appreciates that CMS reinforces in Section 50.2 in the Initial Guidance that quality-adjusted life year (QALYs) will not be considered in negotiation.⁴⁸ Patient groups and governmental bodies such as the National Council on Disability consider use of the metric to be discriminatory towards patients with chronic disease, the elderly, disabled, and other historically marginalized patient populations by placing lower value on their lives and the health gains they may achieve relative to healthier populations. There are better methodologies that assess product value that are more comprehensive, focus on the effectiveness of the product in improving health, and center value on diverse patient perspectives.

For example, Multi Criteria Decision Analysis (MCDA) is a transparent methodology that is increasingly utilized for decision making about health care value. Through an MCDA process, patients are asked what matters most to them, and these weighted factors are the basis for the analysis. As a result, MCDA captures a broader set of value factors in addition to clinical effectiveness, which could include disease severity, potential for a cure, equity, societal value, and caregiver burden. MCDA can be implemented in a way that summarizes the quantitative and qualitative evidence about a product, without simply aggregating quantitative data into one single metric. While MCDA sometimes utilizes QALYs, it can be employed without them.

While MCDA is a preferable approach, another, less-resource intensive, potential approach is the use of cost-consequence analysis (sometimes referred to as an impact inventory or dashboard) to catalog evidence and present it in a way that easily allows for ascertaining all aspects of value. In this approach, all relevant outcomes for the intervention and its comparators are presented in a disaggregated tabular format. This would help facilitate a transparent, value-based assessment and negotiation, especially if it includes the full spectrum of evidence, including traditional clinical outcomes, cost impacts, and societal benefits. This type of approach was recommended by an expert panel convened by USC and the Aspen Institute as a practical,

⁴⁷ Darius N. Lakdawalla *et al.*, *Defining Elements of Value in Health Care—A Health Economics Approach: An ISPOR Special Task Force Report*, 21 *Value in Health* 131-139 (2018), <https://www.valueinhealthjournal.com/action/showPdf?pii=S1098-3015%2817%2933892-5>.

⁴⁸ We also agree that a study should not be completely discarded because it includes QALYs. Studies often contain multiple outcomes, and a QALY metric can be disregarded in favor of a more patient-centered outcome within a single study.

transparent, non-QALY based form of value assessment for the US context.⁴⁹ Determinations on which elements to include could be driven by stakeholder input to mimic the MCDA approach.

We encourage CMS to avoid use of other cost effectiveness metrics that attempt to oversimplify the measurement of value. A single metric that assumes uniform value across patient groups will never reflect the diverse experience of the broader patient community. Furthermore, such metrics are often not transparent in how value is measured, and rarely capture the full value of a product to society. For example, methods that rely on single cost effectiveness metrics do not include aspects of product value such as the impact on health equity, family and caregiver burden, cost savings from reduced hospitalizations and other health care use, and reduced population transmission of infectious diseases.

Lastly, we are concerned that the Initial Guidance provides for limited input from patients and clinicians on what is important in appraising value. This is out of step with best practices in other countries and from groups like ISPOR.⁵⁰ Stakeholder input is critical to ensuring that the methodology and process align with patient preferences and clinical practice. For example, patients should be asked about care preferences and which outcomes matter most to them in line with the MCDA approach described above. Clinicians practicing in the disease area that a selected medicine treats should be engaged to help select clinically appropriate comparators.

* * * *

Gilead hopes CMS will incorporate these suggestions into its revised guidance and implement the MFP Program with a goal of ensuring that it does not disincentivize biopharmaceutical innovation, which could hinder finding a cure for HIV and ending the HIV epidemic. If you have any questions, please do not hesitate to contact Michelle Drozd at Michelle.Drozd2@gilead.com or Laura Okpala at Laura.Okpala@gilead.com.

Sincerely,



Rekha Ramesh
Vice President, Policy
Government Affairs and Policy
Gilead Sciences, Inc.

⁴⁹ Darius Lakdawalla, et. al., *Health Technology Assessment in the U.S. A Vision for the Future*, USC Leonard D. Schaeffer Center for Health Policy & Economics (Feb. 2021), https://healthpolicy.usc.edu/wp-content/uploads/2021/02/Health_Technology_Assessment_in_the_U.S..pdf; see Gillian D. Sanders, et. al., *Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses Second Panel on Cost-Effectiveness in Health and Medicine*, Vol. 316, No. 10, JAMA Clinical Review & Education, (Sept. 13, 2016), <https://jamanetwork.com/journals/jama/articlepdf/2552214/jsc160017.pdf>; Rachael Hunter, et. al., *Cost-consequences analysis - an underused method of economic evaluation*, National Institute for Health Research (2019), <https://www.rds-london.nihr.ac.uk/wp-content/uploads/2018/09/Cost-consequences-analysis-an-underused-method.pdf>.

⁵⁰ Richard Z. Xie, et. al., *Early Reflections on Stakeholder Engagement in Economic Model Development to Inform Value Assessment*, Vol. 8, No. 2, Value & Outcomes Spotlight (March/April 2022), <https://www.ispor.org/publications/journals/value-outcomes-spotlight/vos-archives/issue/view/moving-the-needle-on-health-policy-focus-on-outcomes-based-care/early-reflections-on-stakeholder-engagement-in-economic-model-development-to-inform-value-assessment>.

GSK Comment Letter

Response to CMS Initial Memorandum: Medicare Drug Price Negotiation Program



April 14, 2023

Via electronic submission: IRARebateandNegotiation@cms.hhs.gov

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Deputy Administrator Seshamani:

GSK appreciates the opportunity to comment on the initial memorandum for the Medicare Drug Price Negotiation Program. GSK is a global biopharmaceutical company with the ambition and purpose to unite science, technology, and talent to get ahead of disease together. We seek to prevent and treat disease with vaccines, specialty, and general medicines.

GSK supports policy solutions that transform our U.S. healthcare system to one that rewards innovation, improves patient outcomes, and achieves higher value care. As the Centers for Medicare & Medicaid Services (CMS) implements the Medicare Drug Price Negotiation Program, we are concerned that CMS' policies will adversely impact meaningful innovation, create operational challenges, and limit patient access to transformative therapies.

GSK is a member of and endorses the comments of the Pharmaceutical Research & Manufacturers of America (PhRMA) and the Biotechnology Innovation Organization (BIO) on the Medicare Drug Price Negotiation Program. We respectfully submit the additional comments below to highlight issues of paramount interest to GSK and the patients we serve.

We make the following recommendations for addressing our concerns:

- Set the maximum fair price (MFP) at or near the statutorily mandated ceiling price for any vaccine products selected for Medicare negotiation;
- Improve and clarify the ways Primary manufacturers provide access to MFP by either removing the 14-day requirement or clarifying that the 14-day requirement is after patient eligibility has been verified, and using WAC as the basis for determining MFP discounts/rebates; and
- Ensure that evidence used in determining pharmaceutical therapeutic alternatives for each selected drug is scientifically rigorous, and that experts – including manufacturers and clinicians – are engaged as central resources in this determination.

Below are our recommendations with supporting rationales:



I. Value of Vaccines and Setting the MFP

Vaccines are a public health tool that deserve unique considerations that are not similarly contemplated for other classes of biologics or drugs. Specifically, vaccines are preventive in nature, have benefits seen at a population health level, and typically have durable effects. As a matter of public health policy, maximum uptake of vaccines should be encouraged to minimize the burden of preventable diseases and illnesses and to address health inequities. GSK is concerned that Medicare negotiation for vaccines will disincentivize innovation in infectious and emerging disease – an area that historically has less investment than others¹.

The Centers for Disease Control and Prevention (CDC) sets the US adult and childhood immunization schedules based on recommendations from the Advisory Committee on Immunization Practices (ACIP). FDA-approved vaccines undergo a rigorous evaluation of safety and effectiveness, disease severity, economic analyses, and other factors through ACIP's vaccine recommendation process. Subjecting ACIP-recommended vaccines to Medicare negotiations, after they have already undergone rigorous analyses by experts, could reduce incentives for the development of new vaccines for current and future public health threats. ***Given the unique circumstances of vaccines, GSK recommends that if a vaccine product is selected for negotiation, CMS set the MFP at or near the statutorily mandated ceiling price.***

It is important to note that vaccines are treated differently than biologics and drug products throughout the Inflation Reduction Act (IRA). Under section 1194(c), the applicable percent for vaccines is described with short-monopoly drugs at 75% and vaccines approved under Section 351 of the Public Health Service Act are expressly excluded from the definitions of extended-monopoly and long-monopoly drugs.² Additionally, Medicare beneficiaries already experience no cost-sharing for vaccines covered by both Part B and Part D as a method of encouraging higher utilization that reduces short- and long-term costs for the Medicare program. Therefore, Medicare negotiation for low-cost, high-volume vaccines will have little to no effect on Medicare beneficiary access because beneficiaries are not subjected to out-of-pocket costs for vaccines.

While several critical therapeutic areas, including oncology, HIV, and rare diseases, warrant special consideration, at a minimum, we urge CMS to recognize the unique importance of vaccines when setting MFPs, given their remarkable public health benefit.

II. Improve and Clarify Ways to Effectuate MFP to Maintain Program Integrity

CMS proposes to effectuate the MFP price for selected drugs during the initial price applicability year (IPAY) 2026 by requiring Primary Manufacturers to either ensure the price paid by the dispensing entity is no greater than the MFP or a retrospective reimbursement for the difference between acquisition costs and the MFP. Under the retrospective reimbursement method, CMS proposes to require the Primary Manufacturer provide the payment difference within 14 days.

GSK recommends CMS either remove the 14-day requirement or clarify the 14-day requirement is after a Primary Manufacturer has verified the patient is an MFP-eligible individual. The 14-day requirement is not feasible to process rebates to effectuate the MFP price after the drug has been

¹ [Innovation policy and the market for vaccines - PMC \(nih.gov\)](#)

² Inflation Reduction Act of 2022



dispensed. GSK must verify MFP eligibility for Medicare beneficiaries before issuing rebates. Not doing so could result in duplicate discounts given the lack of access to proper data sets to determine a patient's status for a dispensed drug. The 14-day requirement brings increased risks to program integrity as it relates to MFP and 340B duplicate discounts, which are prohibited in the IRA.

However, GSK will be able to provide a rebate to effectuate the MFP if manufacturers are granted flexibility to provide the reimbursement difference after verification occurs. CMS could partner with a third-party administrator (TPA) to establish a standard invoicing cycle with appropriate validation and payment processing timelines. A comparable process exists, and has been successfully implemented, for the Part D Coverage Gap Discount program, in which Palmetto GBA serves as the TPA. Allowing CMS or manufacturers to establish a third-party administrator to serve as a clearinghouse to effectuate the MFP will improve data integrity and processing timelines.

In addition, **GSK recommends CMS clarify that Wholesale Acquisition Costs (WAC) will be used as the basis to determine MFP discounts/rebates.** CMS provides Primary Manufacturers the option to provide rebates "for the difference between the dispensing entity's acquisition cost and the MFP."³ Manufacturers do not normally sell direct to pharmacy locations. Instead, manufacturers sell products at WAC to wholesalers and distributors who then resell the product to pharmacy locations. A pharmacy's Actual Acquisition Cost (AAC) will likely not equal the cost for which the manufacturer sold the product. Use of AAC as the basis to determine MFP rebates may result in higher base prices than the list prices the manufacturer used for the sale of the drug. Manufacturers are not able to validate the AAC and varied cost bases will result in inconsistent MFP rebates paid for the same product to different pharmacies. AAC may include any third-party markups from entities in the supply chain that will inflate the price and result in higher rebates than required to effectuate the MFP. WAC is a published list price set in advance and available to all entities in the supply chain. The use of WAC as the basis will ensure accurate effectuation of the MFP.

We urge CMS to take specific steps – including either removal of the 14-day requirement or additional clarity on verification of MFP eligibility and the use of WAC as the basis for determining MFP discounts/rebates – to appropriately effectuate the MFP and maintain integrity of the negotiation program.

III. Engage Experts and Proactively Seek Stakeholder Input on Identifying Therapeutic Alternatives

For IPAY 2026, CMS proposes to identify the selected drug's FDA-approved indications that are neither excluded from coverage nor otherwise restricted, and then identify pharmaceutical therapeutic alternatives for each indication of the selected drug, using manufacturer-submitted data, widely accepted clinical guidelines, and peer-reviewed studies. CMS proposes to review existing literature and real-world evidence (RWE), along with conducting its own internal analytics. **GSK recommends that CMS carefully consider the totality of evidence when identifying therapeutic alternatives, including clinical trials and pre-/post-approval real-world evidence that inform appropriate comparators.** CMS should take a methodologically rigorous, data-driven, and patient-centered approach based on the standard of care and clinical decision-making to reviewing evidence. CMS should strictly avoid any bias that could impact therapeutic alternative selection and MFP determination.

³ CMS. "Medicare Drug Price Negotiations Initial Memorandum." Pg. 32. March 15, 2023.

Response to CMS Initial Memorandum:
Medicare Drug Price Negotiation Program



GSK believes that experts, including manufacturers and clinicians, should be included as additional resources for providing clinical confirmation of identified evidence used in determining therapeutic alternatives, and that CMS should go beyond what the Agency laid out in the Guidance to engage key stakeholders in the selection of therapeutic alternatives. Manufacturers are in a strong and unique position to inform CMS' determination of appropriate therapeutic alternatives for a selected drug, based on their extensive expertise and research on the benefits and impacts of their medicines throughout the product lifecycle. In addition, manufacturer-sponsored research frequently includes comparative effectiveness research, which requires selection of a clinically appropriate comparator. Clinicians with disease-specific expertise and disease-specific clinical guidelines generated by clinicians should also play a role in CMS' determination of a selected drug's therapeutic alternatives.

It is procedurally unclear when CMS will identify the therapeutic alternatives for a selected drug and communicate that information to the manufacturer. ***GSK strongly recommends that CMS publicly identify the therapeutic alternative selected, allow manufacturers sufficient time to review any additional research conducted by the Agency, as well as additional submissions from other stakeholders.***

We encourage CMS to carefully consider the totality of evidence when selecting therapeutic alternatives, to make therapeutic alternative selections public, and to allow for sufficient time to review agency research and stakeholder submissions.

GSK appreciates the opportunity to provide comments on the Medicare Drug Price Negotiation Program. We stand ready to engage with CMS on this critical work to ensure the program is implemented without adverse impacts to innovation and, most importantly, Medicare beneficiaries. Please do not hesitate to contact Amy Efantis, Vice President Government Affairs & Public Policy, (Amy.J.Efantis@gsk.com) and/or Harmeet Dhillon, Head of Public Policy, (Harmeet.S.Dhillon@gsk.com), should you have any questions or requests for additional information.

Respectfully,

A handwritten signature in black ink, appearing to read "A. Efantis", is positioned below the word "Respectfully,".

Amy Efantis

Vice President, Government Affairs and Public Policy
GSK



VIA ELECTRONIC DELIVERY to: IRAREbateandNegotiation@cms.hhs.gov

April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244-1850

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026

Dear Administrator Brooks-LaSure:

With the Centers for Medicare & Medicaid Services' (CMS') issuance of its initial set of guidance on implementation of the Inflation Reduction Act of 2022 (IRA), it has become increasingly clear that (a) the IRA has the potential to exact unintended, but catastrophic, consequences for patients with extremely rare conditions; and (b) CMS may not have a sufficient understanding of our communities' unique challenges to steer its policies in a "do no harm" direction. Haystack Project, therefore, appreciates the opportunity to submit its comments on CMS' Initial Guidance.

Haystack Project is a 501(c)(3) non-profit organization enabling rare and ultra-rare (20,000 or fewer US patients) disease patient advocacy organizations to coordinate and focus efforts that highlight and address systemic reimbursement obstacles to patient access. Our core mission is to evolve health care payment and delivery systems with an eye toward spurring innovation and quality in care toward effective, accessible treatment options for all Americans. We strive to amplify the patient and caregiver voice in these disease states where unmet need is high and treatment delays and inadequacies can be catastrophic.

Our comments to the Initial Guidance briefly outline the inherent differences in commercial realities between the treatments our patient and caregivers rely upon and/or hope for and those that address more common diseases and conditions. We also identify specific provisions within the Initial Guidance likely to have unintended consequences for our patient populations as well as actions CMS can take to minimize those consequences.

We ask that CMS fully consider our comments and that it also give Haystack Project and its member organizations the opportunity to meet with IRA-implementation staff and leadership to articulate our concerns in greater detail so that we may work together to protect access to necessary treatments for all patients, regardless of the rarity of their condition(s).

Background: Individuals with Rare and Ultra-Rare Conditions will be Disproportionately Impacted by the IRA's Potential to Deter Innovation.

Although countless lives have been improved or saved by new therapies enabled by Congress' set of incentives for orphan drugs, significant unmet need predominates in extremely rare conditions and rare cancers:

- Of the approximately 7,000 rare diseases identified to date, 95% have no FDA-approved treatment option.
- 80% of rare diseases are genetic in origin, and present throughout a person's life, even if symptoms are not immediately apparent.
- Diagnosing a patient with a rare disorder is usually a multi-year process involving a series of primary care clinicians, specialists, and diagnostic testing regimens – extreme rarity of a disorder compounds the resources required for diagnosis. Patients often progress to more serious and more costly disease states by the time they receive a diagnosis.
- If a diagnosed condition has no FDA-approved option, treatment often involves off-label use of existing products.
- Approximately half of identified rare diseases do not have a disease-specific advocacy network or organization supporting research and development, and lack of disease-specific natural history severely complicates research toward new, targeted treatments.

Patients suffering from rare diseases that are currently untreatable have maintained hope that the incentives toward innovation, coupled with increased scientific understanding of disease mechanisms, would stimulate progress toward treatment and, eventually, a cure. The economic calculation of unmet patient need balanced against research and development costs, projected risk, and population-based revenue estimates must be accompanied by an analysis of whether it is possible to successfully clear reimbursement mechanisms and hurdles that may tip the scales for or against pursuing a specific drug candidate for an orphan indication. For patient populations approaching the 200,000 orphan disease limit, current incentives have proven to be sufficiently robust to mitigate clinical trial and reimbursement risks. As affected populations dwindle below 20,000 or even into and below the hundreds, the balance can be far more tenuous, and risks or uncertainties can discourage the investor interest required to take promising therapeutic candidates from bench to market.

Patients with rare and ultra-rare conditions as well as rare cancers rely on payers and society in general to lay a strong foundation that gives investors a level of comfort that the costs of research and development can be recouped, either through the price of the new drug, its use in other patient populations, or both. Without this, there is little reason for us to hope they will invest their limited resources in advancing the treatments we need.

Haystack Project and its member organizations have focused on educating stakeholders and shaping health policy to address longstanding challenges to treatment access and innovation. We have engaged with CMS through comments on CMMI model proposals, implementation and refinement of the Medicare Quality Payment Program (QPP) and the Affordable Care Act, as well as throughout annual rulemaking cycles refining policies under Medicare Parts A, B, C and D. In 2019, Haystack Project expressed its increasing concerns that health reform efforts initiated to decrease health care costs would fail to consider our patient communities:

We are concerned that drug-pricing reforms will all but close the narrow window for commercial viability of ultra-rare disease treatments. Our sincere hope is that a greater understanding of our experiences will enable pragmatic solutions to existing problems and guide future health system refinements that take our unique needs into account.

Since enactment of the IRA, Haystack Project membership has continued to grow – both in numbers (nearly doubling to 150 ultra-rare disease advocacy organizations) and in the acute sense of urgency on the need to be heard, prioritized and accounted for in the policy decisions shaping treatment access and product development for the foreseeable future. We recognize that the IRA offers financial relief to our patient communities in (1) capping Part D out-of-pocket costs and (2) enabling a “smoothing” mechanism so that patients can spread their out-of-pocket costs over the year. We expect that these Part D refinements will reduce financial stress on patients and their families so that more patients can base their treatment decisions on medical need rather than financial resources.

Unfortunately, the drug price negotiation program presents significant threats to the fragile balance that has historically enabled researchers, manufacturers, and investors to capture an adequate return on investment for

targeted treatments in small population diseases and rare cancers. Haystack Project expects that the drug price negotiation program will marginally reduce healthcare costs for patients with relatively common conditions. The vast majority of ultra-rare disease and rare cancer patients - who routinely hit the out-of-pocket cap in Part D - will not experience any benefit from CMS' drug price negotiation. That is not to say that the program will have no impact on our patients. Haystack Project's community of patients and caregivers fear that unless CMS implements the drug price negotiation program with proactive and intentional consideration of the complex set of incentives and risks inherent to developing treatments in the ultra-rare disease space, the scales will inextricably tip away from innovation.

We ask that CMS:

- Engage in meaningful dialogue with Haystack Project and other patient organizations to identify innovative approaches to accommodate challenges associated with developing rare and ultra-rare disease treatments, including through CMMI and CMS' general demonstration authority.
- Expand the window for stakeholder feedback on the Initial Guidance, and in particular, consider implications for rare diseases.
- Identify 'qualifying single source drug' by NDA/BLA.
- implement the orphan drug exemption to maintain incentives for rare disease drug development and expansion of labeled indications for existing therapies
 - Work with patient and other stakeholders to ensure that access to orphan drugs is not impeded by diversity of rare conditions for which a treatment is safe and effective.
 - Implement a transparent process for manufacturers to submit evidence demonstrating that a particular product is eligible for the orphan drug exception.
 - Identify orphan drug designations for a particular product at the time of selection, not the date on which the product achieved one or more of its FDA approvals.
- Apply the small biotech exception with minimal burden to manufacturers.

Haystack Project urges CMS to expand the window for stakeholder feedback on the Initial Guidance.

Haystack Project engages its member organizations by analyzing and educating its members on new policy proposals likely to impact treatment access and innovation. This enables our communities to contribute general feedback as well as specific examples of how a new policy might impact patients. The Initial Guidance contains a complex set of interconnected proposals and mechanisms that require thorough analysis, substantial knowledge of the drug and biologics manufacturing industry, and significant time to ascertain and convey its impacts to non-industry stakeholders. The 30-day comment period was far too short to enable Haystack Project to collect specific, meaningful input from our member organizations and incorporate the feedback into a comprehensive comment.

In addition, CMS' decision to broadly define 'qualifying single source drug' for negotiation eligibility purposes was unexpected. Haystack Project had anticipated that CMS would identify negotiation-eligible drugs on the basis of NDA/BLA approvals. This decision will shape the IRA drug price negotiation program to negate existing incentives for securing approvals in small population conditions and burden industry stakeholders in a manner not likely contemplated within the statute. The repercussions from CMS' decision are likely far-reaching and, we believe, warrant a level of consideration that cannot be accomplished without stakeholder feedback. We urge CMS to reverse its finalization of Section 30 of the Initial Guidance and solicit additional stakeholder comments on the entirety of the guidance.

CMS Should Reconsider its Definition of Qualifying Single Source Drug

Haystack Project was both surprised and disappointed that CMS' Initial Guidance finalized a definition of qualifying single source drug that looks to active moiety or active ingredient rather than NDA/BLA. We had expected that CMS would look to the statutory language and its reference to products as negotiation-eligible if the product was approved under an NDA/BLA and seven/eleven years have elapsed since such approval. Under CMS' definition, it would be possible to render a drug eligible for which an NDA is approved, for example, 2 years before a product with the same active moiety/ingredient is selected for negotiation. Under any reading of the plain language of the IRA, the product would not be negotiation-eligible.

We have significant concerns that CMS' approach to identifying products eligible for negotiation (and to which any Maximum Fair Price (MFP) would be applied) maximizes the extent to which the IRA's drug price negotiation program will hinder research and development toward expanded labels for existing treatments. Individuals with relatively common conditions will likely maintain access to promising therapies developed for other conditions based on compendia listings for off-label uses. Off-label treatments for extremely small population conditions are rarely included in the various compendia relied upon for Part D coverage, and patient access is completely foreclosed. In fact, Haystack Project has heard from several patient groups that treatments within the standard of care for their ultra-rare condition fall outside the Part D benefit. Unless CMS retracts its determination to include all NDAs/BLAs for a product as a singular qualifying single source drug for negotiation purposes, our patients have little hope that manufacturers be able to justify investing in NDA/BLA approvals for ultra-rare uses of existing treatments.

In addition to the concerns described above, Haystack Project expects that CMS' definition of qualifying single source drug will place burdens on manufacturers that Congress did not consider in drafting the IRA. We note that CMS' set of examples on application of the qualifying single source drug definition included scenarios with multiple NDAs and multiple manufacturers. The Initial Guidance contemplates requiring the primary manufacturer (NDA/BLA holder) to assume full responsibility and liability for participation in the negotiation process, submission of complete, accurate information and access to the MFP.

Agreements between manufacturers are generally based on contracts negotiated and executed before the parties perform any manufacturing, distribution, and/or marketing activities. They outline the duties and responsibilities of the various parties based on the laws and regulations in place at the time of contract execution and may provide for amendment based on specified legal or regulatory changes. Neither the IRA nor CMS' Initial Guidance provide for any mechanism through which a primary manufacturer can secure information or performance from a secondary manufacturer. While CMS might assume that manufacturers can contract with each other to accommodate the IRA requirements, the substantial liability and potential monetary penalties placed on primary manufacturers negates the potential for a level playing field between the parties. We expect that CMS will face legal challenges to this provision of its Initial Guidance and urge the Agency to take a more pragmatic approach. Identifying negotiation-eligible products by NDA/BLA will preserve incentives for research and development of new uses for existing products, and minimize the potential that manufacturers will be responsible for activities over which they have no control.

The Orphan Drug Exclusion Should be Implemented to Maintain Incentives for Developing New Treatments in Rare Conditions and Expanding Labeled Indications of Existing Therapies

Haystack Project appreciates that CMS recognizes the need to protect access to orphan drugs currently available as well as innovations that have yet to be developed. We fully support CMS' determination to qualify drugs for the exclusion based on whether approved indications are within a single designation. Unfortunately, the policy on defining a qualifying single source drug by active moiety/ingredient discussed above will likely reduce manufacturer interest in pursuing multiple indications within or beyond a single designation.

When the IRA was enacted, our member organizations voiced significant concerns that the narrow exception for orphan drugs would introduce a new set of considerations to deter pursuit of FDA approval for multiple uses of promising new therapies. Drug and biotech manufacturers already face considerable pressures to fulfill their legal

obligations to shareholders while maintaining their commitment to improve care for the patient communities they serve. The landscape envisioned under CMS' Initial Guidance increases the tension between those interests. For example, it would be difficult to make a financial case for investing in clinical studies toward approval of an ultra-rare indication outside a product's original orphan designation unless the financial consequences of losing eligibility for the orphan drug exception were outweighed by projected revenue from a new indication. The smaller the population, the less likely it is that the manufacturer could justify investing in the research needed for FDA approval. Any decision to rely on off-label use (for cancer uses and indications likely to be included in compendia) would be more likely driven by math than an intent to game the system. CMS, patients, and manufacturers can and should be aligned on incentivizing (or at least not discouraging) research that maximizes access to innovations across indications through a demonstration of safety and efficacy sufficient to garner FDA approval.

Patients with ultra-rare conditions and rare cancers are particularly concerned that:

- Manufacturers will face pressures to focus on an orphan indication with the largest patient population.
- Research and development programs confirming clinical benefit for accelerated approval treatments may be halted and indications withdrawn if those indications fall outside a single orphan drug designation. We note that on April 6, 2023, AbbVie and Johnson & Johnson announced withdraw of the accelerated approvals for Imbruvica (ibrutinib) in mantle cell lymphoma (MCL) and marginal zone lymphoma (MZL). Patients with these rare cancers will have only one BTK inhibitor available to treat their disease.
- Pressures to focus on larger-population orphan designations/indications could delay product approval and increase initial research and development costs. The BTK inhibitor described above was approved for MCL a year before receiving approval in chronic lymphocytic leukemia (CLL).
- The IRA's chilling effect on research and development will fall disproportionately on patients with ultra-rare diseases and rare cancers.
- Investors and shareholders will seek to ensure that initial price points for newly-approved drugs are sufficient to recoup research and development costs and achieve a profit margin from successful innovations.

Once again, we appreciate that CMS has limited discretion in implementing the orphan drug exclusion and that the Agency seeks stakeholder feedback on how it might implement the IRA drug price negotiation program without deterring access and innovation in rare diseases. We urge CMS to:

- Work with patient and industry stakeholders to remove the single orphan designation requirement from the IRA orphan drug exception.
 - o The existing statutory language will severely chill research and development to secure approval for ultra-rare disease uses of existing orphan drugs.
 - o The set of compendia used to determine whether a use is medically accepted (and, therefore, a covered Part D drug) tend not to include off-label uses in ultra-rare conditions.
 - o Ultra-rare patients can find that treatments that are part of the standard of care are not within the Part D benefit *for patients like them* simply because their condition is too rare to catch the attention of drug compendia listings.
- Identify qualifying single source drugs by NDA/BLA (as more fully outlined in the preceding section).
- Engage in meaningful dialogue with Haystack Project and other patient-centered organizations to preserve the balance in incentives and risks that has spurred innovation in rare and ultra-rare disease treatments, including through CMMI and CMS' general demonstration authority.

- Implement a transparent process for manufacturers to submit evidence demonstrating that a particular product is eligible for the orphan drug exclusion.
- Identify orphan drug designations for a particular product at the time of selection, not the date on which the product achieved one or more of its FDA approvals.

The Small Biotech Drug Exception should be Applied with Minimal Burden to Manufacturers.

Haystack Project understands that CMS has been charged with implementing the Inflation Reduction Act provisions related to price negotiation, including the small biotech exception, as Congress directed. In our comments to the Information Collection Request associated with the Small Biotech Drug Exception, we asked that CMS to exercise its implementation discretion to minimize the IRA's potential to disrupt the fragile balance between risk and reward that has fueled hope for new treatments within our patient communities. We reiterate our recommendation that CMS provide stakeholders with greater clarity on the process it will use to determine eligibility for the small biotech drug exception, including that the Agency:

- Ensure that manufacturers know how and when they will be informed of CMS' receipt of a submission and determinations on completeness and eligibility for the exception. CMS' communication could be by email, letter, or other mechanism, but it is essential that manufacturers know what they are looking for and when to look for it.
- Provide a substantive response to submissions when it determines that a small biotech manufacturer's drug is ineligible for the exception. The response should be sufficiently detailed to enable manufacturers to provide any data or other information that may refute a negative CMS determination.
- Implement a dispute resolution process that manufacturers can understand and utilize in the event of a negative determination.
- Accept manufacturer submissions through a dedicated email "inbox." Haystack understands that CMS envisions developing an HPMS tool that manufacturers would use to submit information on the Small Biotech Exception ICR form. Unfortunately, creating new processes within short implementation timeframes increases the likelihood for delays, errors, and inadvertent inclusion or exclusion of information. Emailed submissions with automated receipt response will give manufacturers confidence that the information they intended to send was received.
- Maintain open lines of communication between specific CMS personnel making determinations on small biotech drug exception eligibility and manufacturers submitting information to qualify their drugs. Our patient and caregiver communities know all too well that the decisions on our access to treatments are often made within closed processes that do not include our participation. The IRA implementation processes are new to industry, patients, and CMS, and are therefore vulnerable to miscommunications, inadvertent submission errors, and other missteps that could prove dispositive. A clear and open line of communication between CMS staff and manufacturers can avoid unintended delays and erroneous determinations.
- Streamline continuing eligibility for the small biotech drug exception. Under the IRA, a drug determined to be eligible for the exception would lose its eligibility only if the manufacturer is acquired by a manufacturer that does not qualify for the exception. We urge CMS to apply the exception to drugs for each year upon receipt of a simple statement certifying that the manufacturer has not been acquired by another entity. A new eligibility submission should only be required when an acquisition has occurred, and the new manufacturer seeks to qualify for the exception.

- Allow for small biotech drug exception submissions in each year for which the exception is applicable. This will permit companies that failed to fully submit required information within the timeframe allowed to secure the exception for the drugs it was intended to benefit.
- Furnish a material response to submissions indicating whether the submission was successful. The response should (as noted above) provide a clear and substantive rationale for CMS' decision if the Agency determines that the drug is ineligible for the small biotech drug exception.

Haystack Project has previously expressed its concern that CMS' ICR and the explanations accompanying it did not fully implement the IRA small biotech drug exception. We urge CMS to modify its "form" for small biotech drug exception qualification to fully comply with the statutory two-pronged "test" conferring eligibility when drugs meet **either** prong. This means that a drug would be eligible for negotiation applicable to Part D drugs if it meets either the 1%/80% test on Part D expenditures or the 1%/80% test on Part B expenditures.

Conclusion

Haystack Project appreciates the opportunity to submit feedback on the Initial Guidance toward implementing the drug price negotiation program within the IRA. Our member organizations have significant concerns that the decisions CMS makes within the next several months could determine the set of new treatment options in ultra-rare conditions and rare cancers for the foreseeable future. More importantly, the decisions likely to have the greatest impact are being made without a meaningful engagement and dialogue between CMS and the rare and ultra-rare disease community.

We would appreciate the opportunity to meet with IRA implementation staff and leadership to further discuss the concerns within our communities and possible mechanisms to address them, such as:

- Including patient-centered value considerations within the negotiation process.
- Ensuring that the importance of a particular treatment in a rare or ultra-rare condition is not lost within the context of its use in a relatively common condition with multiple available treatment options (i.e., averaging benefit across uses marginalizes the health care needs of ultra-rare patients).
- Incorporating value-based payment arrangements into the drug price negotiation process.
- Developing mechanisms to encourage (carrots rather than sticks) manufacturers to apply discounts throughout a product's lifecycle – not just for Medicare patients after the product has been selected for negotiation.
- Additional ideas within our member organizations to foster innovation and treatment access for patients with ultra-rare conditions and rare cancers.

Once again, we thank you for your consideration of our comments and look forward to a substantive discussion to ensure that all Medicare beneficiaries have access to the treatments they need. In the meantime, if you have any questions, please contact me or our policy consultant M Kay Scanlan, JD at 410.504.2324.

Very truly yours,







Alagille Syndrome Alliance
Stay strong. Press on.



Submitted electronically to IRAREbateandNegotiation@cms.hhs.gov

April 14, 2023

Chiquita Brooks-LaSure, MPP
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
P.O. Box 8016
Baltimore, MD 21244

Re: Comments to the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments Dated March 15, 2023.

Administrator Brooks-LaSure,

Thank you for the opportunity to respond to the Initial Memorandum issued on March 15. As shared in our meeting on February 3 and through our subsequent letter, we believe Distributors are well positioned and willing to address the supply chain challenges that will result from implementation of the Maximum Fair Price (MFP) Manufacturer Discount Program.

As you know, Healthcare Distribution Alliance is the national trade organization representing primary pharmaceutical Distributors whose members ensure the safe and efficient distribution of prescription medications to healthcare providers and the patients they serve. Our members are the vital link between the nation's pharmaceutical Manufacturers and more than 300,000 pharmacies, hospitals, physicians, clinics, long-term care facilities, durable medical equipment providers, and others nationwide.

As noted in our letter of February 28 and our earlier meeting, a retrospective claims-based chargeback discount process could leverage existing industry chargeback capabilities for Manufacturers to provide Dispensers access to MFP; however, there are gaps in today's data flows that must be overcome, in particular, claims data is required to operationalize a claims-based chargeback discount process.

Our comments to the Initial Memorandum are focused on the administration of the Manufacturer discount program as discussed in Sections 40.4 and 90.2 which deal with providing and monitoring access to the MFP. The Initial Memorandum emphasizes Part D claims, so we have tailored our responses in similar fashion. However, our comments also apply to Part B claims, which will have additional complexities and nuances. Our comments reflect our role as Distributors as well as our interest in ensuring that our pharmacy, physician, and other provider customers have access to the MFP.

If Manufacturers choose to pursue a claims-based chargeback discount process, we believe the result would need to be a unified solution that would handle Part B and Part D claims ensuring that discounts flow efficiently from Manufacturer, to Distributor, to Dispenser. It must be noted that none of these entities currently has in place the full infrastructure required for a claims-based chargeback process. Without clear, consistent CMS policy and a willingness by CMS to perform those roles in the process that it is best suited to, it will be difficult for industry stakeholders to justify the investments needed and could lead to serious delays.

1. Manufacturer's Obligation to Provide Access to the MFP

CMS guidance states and emphasizes that the Manufacturer must provide Dispensers with access to the discounted price. We interpret that emphasis to indicate that CMS may not intend to contract a Third-Party Administrator believing that industry can administrate the program alone. CMS must reconsider such a position. A worst case scenario would be for individual Manufacturers to develop separate systems and processes creating multiple inefficiencies across the industry and increasing overall healthcare costs. CMS is best positioned to perform certain crucial roles needed for the industry to adopt a unified solution that is effective and efficient, therefore CMS must perform those roles. We will continue working with Manufacturers and channel stakeholders as they evaluate the potential adoption of a claims-based chargeback process to provide access to the MFP. As noted in our letter of February 28, providing accurate, timely claims-based chargebacks to Dispensers would require accurate and timely claims data from the payors.

Key Point: A claims-based chargeback discount process could effectively provide Dispensers access, given that Medicare or its contracted entities supply claims data.

2. Not Burdening Dispensers to Access MFP

CMS guidance uses an example of a pharmacy initiating a chargeback request to its Distributor to receive the Manufacturer discount. However, relying on Dispensers to initiate the discount process would be problematic. First, Dispensers do not typically provide claim information to Distributors. Secondly, our Distributor members, who provide many support programs for providers and pharmacies, have firsthand experience with the limitations in the systems and business processes used to operate these small practices. For example, some systems cannot accurately report claim reversals as a post-adjudication function. Requiring Dispensers to perform additional steps to initiate the discount process would require significant modifications to the systems that operate their businesses. It would add needless cost and complexities to administering the discount program. Putting this burden on Dispensers could create financial chaos for small providers and pharmacies, potentially leading to beneficiary disruption. Instead, the Manufacturer Discount Program should be triggered automatically by the claims process without manual intervention by the pharmacy or physician's office.

The statute intrinsically defines the Manufacturer Discount Program as an integral part of the claims process. Likewise, we strongly believe that leveraging the automated, reliable claims process is integral to implementing the program. Dispensers should access the MFP via claims data from Medicare's Contracted Entities.

Key Point: CMS should not burden Dispensers to initiate the claims-based chargeback process; it should be triggered automatically by the Part B and Part D claim approvals.

3. Fundamental Requirements for an Effective Chargeback Discount Process

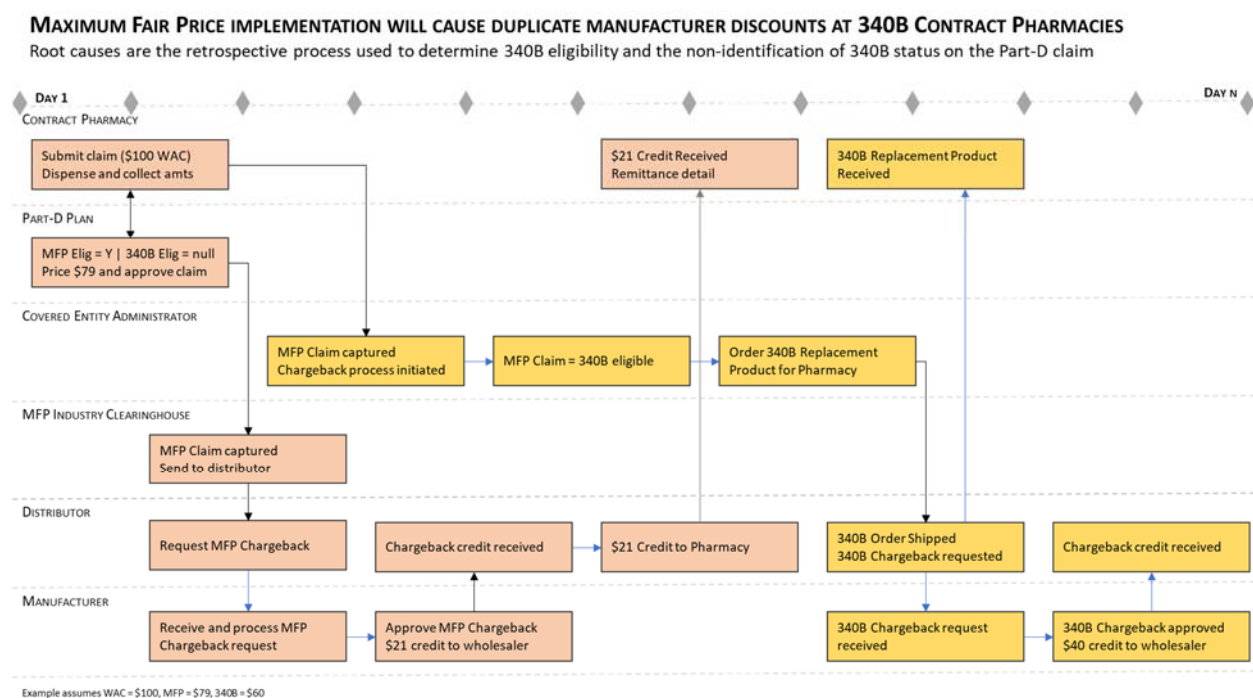
We believe both Dispensers and Manufacturers, with the direction and oversight of CMS, would consider an industry-operated claims-based chargeback process to be a credible and dependable

way to provide access to the MFP. This is true, however, only to the extent that stakeholders trust the integrity and validity of the claims data. This data must be timely, accurate, and complete. Claims, reversals, and rebills are all crucial transactions to accurately administer discounts. Furthermore, paper claims still occur, as do “offline” adjustments by Plan D Sponsors, such as Dispenser audits. These nuances are not available in any data source other than the payor’s claims data. This data can be provided in PDE format or other NCPDP standard format. Furthermore, to meet the 14-day requirement for Part D, the data should be made available no less frequently than daily to allow ample time for Distributors and Manufacturers to each perform their respective role.

Key Point: CMS-contracted entities are the authoritative, best source for trusted data essential to the discount program. CMS guidance should ensure their full cooperation.

4. Preventing Duplicate Discounts when 340B Ceiling Price is Lower Than MFP

Without additional guidance from CMS, 340B-eligible claims dispensed to MFP-eligible patients *WILL* result in duplicate discounts for MFP products, in particular at 340B Contract Pharmacies. There are two root causes of this issue. First, at the point of sale, a Contract Pharmacy does not know if a prescription qualifies for 340B. This typically happens days later by the 340B Contract Administrator hired by the 340B Covered Entity. Second, while current NCPDP claim standards include a 340B indicator, it is generally not used today even when patient eligibility is known due to the concern that the Part-D Sponsor would base reimbursement on the 340B ceiling price.



Example of Duplicate Discounts

The graphic above illustrates the issue. It assumes a 2026 dispense to an MFP-eligible beneficiary for an MFP-selected product. The Part D Sponsor has approved the claim and correctly calculated patient out-of-pocket costs. The submitted claim triggered a chargeback request of \$21 that is approved by the Manufacturer and flowed from the Distributor to the Pharmacy. During that process the Administrator hired by the Covered Entity has uploaded the pharmacy’s claims and identified this claim as 340B eligible and automatically reordered 340B replacement stock shipped to the Contract

Pharmacy and billed it to the Covered Entity. As a result, the Manufacturer has issued two discounts, a \$21 MFP discount and a \$40 340B discount.

Key Point: Current practices, if unchanged, will result in duplicate discounts.

While existing NCPDP claim standards allow a pharmacy to prospectively indicate that the product being billed is purchased under 340B rights (see below), use of the indicator is limited. A key barrier to its use is the concern expressed by Covered Entities that identifying the claim as 340B would lead to Part D Sponsors reducing reimbursement to the Covered Entity basing it on the 340B price rather than the WAC or MFP. Perhaps CMS could offer guidance on this issue. From the perspective of the claims-based chargeback process, use of the indicator would result in no chargeback request to the Manufacturer and no duplication.

The NCPDP standard uses the Submission Type Code [Field D17-K8] with a value of AA for this purpose. The value AA indicates that “*prior to providing service, the pharmacy has determined the product being billed is purchased pursuant to rights available under Section 340B of the Public Health Act of 1992 including sub-ceiling purchases authorized by Section 340B (a)(10) and those made through the Prime Vendor Program (Section 340B(a)(8))*”.

The other barrier to adoption of the prospective 340B indicator is the nature of Contract Pharmacy arrangements where the 340B status of the claim is unknown at the point of sale and determined retrospectively by the 340B Administrator. If CMS were to require use of the 340B indicator it would force the Administrator to modify its processes that reorder and ship 340B replacement product to the Contract Pharmacy to not reorder replacement product for an MFP Product unless the 340B indicator appears in a claim. The modified process would first notify the Contract Pharmacy to reverse the claim and resubmit the claim with the 340B indicator. Once the Administrator detects the 340B indicator in the resubmitted uploaded claim, it would then reorder the 340B replacement product. Note that in this sequence, the initial claim would auto-trigger the MFP discount process, however, the reversal of the claim would also trigger the MFP discount process and would offset the earlier claim, eliminating the MFP discount. The resubmitted claim would also trigger the chargeback process, but due to the presence of the 340B indicator it would not be forwarded to the Manufacturer for an MFP discount. It should be stressed, however, that the administrative process of claim reversals and resubmittals could be quite burdensome for the Contract Pharmacy. Plus, each time a claim is resubmitted the 14-day payment window resets to the newest claim date impacting the cash flow of the Contract Pharmacy.

Key Point: Use of the 340B indicator could eliminate duplicate discounts, but existing barriers to use of the indicator remain high.

Given the barriers to use of the 340B indicator in the claim, a retrospective process that eliminates duplicate discounts could be part of the claims-based chargeback process. This would require the 340B Contract Administrator (on behalf of the Covered Entity) to upload the 340B claims to the chargeback process. The 340B claims would be matched against the claims that entered the chargeback process automatically after claim submittal. Duplicates discounts would be identified, causing the chargeback process to send an MFP chargeback reversal to the Manufacturer and the Dispenser eliminating the duplicate discount. The retrospective process would also properly account for claims that might contain the 340B indicator. In other words, the retrospective process does not preclude any use of the prospective process, they could work in tandem. This retrospective process would rely on the obligation for the timely and accurate submission of the 340B claims data.

Key Point: Adding a 340B retrospective claims process to the claims-based chargeback process would eliminate duplicate discounts and avoid the barriers to the 340B indicator.

5. Nonduplication when 340B Ceiling Price is Higher Than MFP

If the MFP of a selected drug is lower than the 340B price, the Manufacturer must provide the Covered Entity with access to the lower MFP. In other words, the Covered Entity is owed the difference between the MFP and the 340B ceiling price. The claims-based chargeback process could accurately act upon claims that meet this condition if the 340B indicator is populated. To illustrate this point, assume the MFP=\$50 which is lower than the 340B \$60 price. The 340B claim would automatically enter the claims-based chargeback process. The process would detect that the MFP is lower than the 340B price and initiate an MFP chargeback request to the Manufacturer for \$10. This chargeback would flow from the Manufacturer to the Distributor to the Covered Entity. The retrospective process described above with the obligatory uploading of 340B claims by the Covered Entity into the claims-based chargeback process could also handle this scenario.

Key Point: Retrospective reporting of 340B status would also comply with the “lesser of” discount requirement in the claims-based chargeback process.

6. Discussion on Transparency and Complaints

CMS anticipates that pharmaceutical database companies such as the drug compendia First Databank and Medi-Span will publish the MFPs, making them readily accessible to pharmaceutical purchasers, and that such transparency will help dispensing entities and eligible individuals to know the MFP for a selected drug and determine whether they are able to access it. This seems reasonable. We recommend that CMS publishes NDC numbers along with the list of MFP drugs. Beneficiaries will have NDC numbers readily accessible on their printed prescription materials. The NDC list would also help Plan Sponsors, Distributors, and Dispensers ensure accurate handling.

Key Point: CMS should include NDC numbers when publishing the list of MFP drugs.

7. Complaints from Beneficiaries

CMS intends to establish a process for beneficiaries, dispensing entities, and other providers and suppliers to report instances when the MFP should have been made available to them but was not. We believe CMS should look at the processes for Beneficiaries and Dispensers through separate lenses. In our opinion, reported patient incidents will most likely be related to other issues a beneficiary may experience in the Medicare program. For example, beneficiaries may have not received the MFP due to other issues that Medicare staff is already experienced in dealing with, such as lapsed coverage, outstanding premiums or specific plan nuances. Therefore, we recommend these complaints are handled by existing CMS staff and processes.

Key Point: Use Medicare’s existing complaint mechanisms for Beneficiaries.

8. Complaints from Dispensers

We believe that Manufacturers (and Distributors in a claims-based chargeback process) will act in good faith to implement the new CMS guidelines for MFP. Consequently, we anticipate that Dispensers’ complaints will also be dealt with in good faith. Complaints that may arise will be complex and likely reflect a misunderstanding of the new guidelines on the part of the Dispenser. Dispensers fill thousands of Medicare claims each year; would CMS accept a complaint of an individual claim where the Plan Sponsor properly applied MFP but the Dispenser is uncertain they received the retrospective discount? An alternative would be for each Manufacturer to state how Dispensers can file complaints with them. CMS may want to offer an appeals process, but should require that Dispensers first use the Manufacturer’s designated complaint process which would resolve nearly all issues.

Key Point: CMS should ask Dispensers to make reasonable efforts to first resolve the issue with its trading partners prior to appealing to CMS.

9. Discussion on Secondary Products

CMS guidance discusses the responsibilities of a Primary Manufacturer to ensure the MFP is available for a selected drug with Secondary Manufacturers. In our opinion, it is unlikely that a Dispenser or patient would experience the issue described in the guidance. Again, we believe that Manufacturers will act in good faith to implement the Manufacturer Discount Program. In the example from the guidance, there is a selected product from a Primary Manufacturer, yet there is no MFP on the same product from the Secondary Manufacturer. This oversight would be exposed to the industry at large as soon as CMS publishes the list of selected drugs with NDCs and would likely be resolved prior to launch date.

Similarly, CMS points out that it is possible for an entity to purchase one or more drug or biological products included in the selected drug from a Distributor, repackage or relabel such products, and then re-market them pursuant to one or more NDA(s) or BLA(s) included in the selected drug. CMS believes that the MFP should be made available to eligible individuals and Dispensers.

The success of the discount program will depend on efficient and effective processes that do not rely on individual actions but are auto triggered and automated. In this vein, the importance of drug identifiers cannot be overstated. The list of selected products must be reduced to a list of NDC identifiers for use by all stakeholders.

Key Point: The authoritative list of NDCs should be maintained by CMS and made available to Plan D Sponsors, Dispensers, and all industry stakeholders.

10. Summary

We believe that CMS cannot rely solely on industry to implement the discount program. While Distributors believe a claims-based chargeback process is viable with appropriate data access, it cannot be accomplished without CMS, who must lead to ensure the industry is able to adopt a unified solution that works for all industry stakeholders and avoids any beneficiary disruption.

This leading role should ensure that:

- A single, consistent, unified solution for Part B and Part D is developed.
- CMS performs the crucial roles that it is best positioned to perform, such as administering the timely, accurate and complete collection of claims data from its contracted entities.
- A claims-based chargeback process can rely on Medicare and its contracted entities.
- Dispensers should not be burdened to initiate the claims-based chargeback process; it should be triggered automatically by the Part B and Part D claim approvals.

Implementing a claims-based chargeback process will require both public and private investments. The industry may still need its own intermediary to fully execute a claims-based chargeback process, but that intermediary would not be a substitute for those roles best suited to CMS. We believe that Manufacturers will fully evaluate the benefits and viability of a claims-based chargeback process and we stand ready to assist them in that evaluation. Those benefits include purchasing and acquisition costs records as well as the broad contractual and financial relationships Distributors have in place with more than 300,000 pharmacies, hospitals, physicians, clinics, long-term care facilities, durable medical equipment providers, and others nationwide.

We believe 2026 is achievable with suitable advanced planning. All industry participants—including Manufacturers, Distributors, Dispensers, and Medicare’s Part D and Part B Contracted Entities—will require lead time to design, plan, test, and modify systems. As Distributors, we are willing to do our part, if called upon, to assist CMS and Manufacturers in administering the discount program and ensuring that our Dispenser customers and their patients have timely and accurate access to MFP.

We appreciate being a resource for Medicare and are continuing our early readiness efforts.

Sincerely,

A handwritten signature in black ink, appearing to read "Patrick M. Kelly". The signature is fluid and cursive, with the first name "Patrick" and last name "Kelly" being more prominent than the middle initial "M".

Patrick Kelly
Executive Vice President, Government Affairs



April 14, 2023

Meena Seshamani, MD, PhD
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program Guidance

Dear Deputy Administrator Seshamani:

The Healthcare Leadership Council (HLC) thanks the Centers for Medicare & Medicaid Services (CMS) for the opportunity to submit comments on CMS' initial guidance for the Medicare Drug Price Negotiation Program for Price Applicability Year 2026.

HLC is a coalition of chief executives from all disciplines within American healthcare. It is the exclusive forum for the nation's healthcare leaders to jointly develop policies, plans, and programs to achieve their vision of a 21st century healthcare system that makes affordable high-quality care accessible to all Americans. Members of HLC – hospitals, academic health centers, health plans, pharmaceutical companies, medical device manufacturers, laboratories, biotech firms, health product distributors, post-acute care providers, home care providers, and information technology companies – advocate for measures to increase the quality and efficiency of healthcare through a patient-centered approach.

Lowering the out-of-pocket costs consumers pay for prescription drugs and ensuring that consumers can manage those costs over the plan year is a top priority for HLC members. We appreciate CMS laying out the requirements and parameters of the Negotiation Program included under Sections 11001 and 11002 of the Inflation Reduction Act (IRA). In response, HLC offers the following comments on what we identify as problematic provisions within the IRA, as well as the initial guidance which undermines biopharmaceutical innovation and patient access to next generation therapies.

Transparency

HLC encourages CMS to develop guidance and rules that are open and transparent, and provide meaningful opportunities for stakeholder input. The IRA includes vague standards for government price settings and gives CMS wide latitude to implement those provisions. In particular, the law sets tight deadlines for implementation, far shorter than other major healthcare legislation. It also allows CMS to implement policy changes through program instruction or guidance, rather than traditional rulemaking that gives stakeholders adequate time to digest and respond thoughtfully to any major proposed policy changes. We urge CMS to work more collaboratively with the private sector to discuss and recommend alternative solutions to arrive at the same goal.

Patient Access and Part D Redesign

HLC believes government price controls will have a negative impact on the Medicare Part D program which reaches beyond the specific number of drugs selected for price setting and results in patients losing access to their medicines. Specifically, we believe price setting one selected drug could impact other therapeutic competitors in the same class of medicines. In addition, we are concerned that the downstream effects of price setting will reduce consumers' choice of plans and formularies in Part D. Beneficiaries enjoy a broad array of plan choices in Part D, including different formulary options.¹ As more prescription drugs are subject to Maximum Fair Pricing (MFP), the ability of plans to differentiate from one another will decrease and lead to fewer choices in plans or formulary distinctions for consumers. Furthermore, with fewer plan choices and thus less competition, we are concerned that premiums will increase.

Reference Pricing Standards

CMS proposes to base its decision making on standards of therapeutic "reference pricing," which is controversial and often results in judgments that are clinically inappropriate and disregard the needs of patient subgroups. The requirement of a therapeutic alternative that is similar to the selected drug often overlooks significant differences in the needs of patients, as many alternative therapies do not fit within broad judgments of clinical similarity. We believe this metric which is relied upon by the Department of Veterans Affairs is not appropriate for care delivered in a broader community setting compared to special populations who receive care in closed healthcare delivery systems.

We are also concerned the proposed definition of "unmet needs" is too narrow. The definition proposes to restrict these unmet needs only for diseases for which there are limited or no treatment options available. Such a narrow definition devalues medicines that help address patient needs and could result in worse health outcomes for individuals who don't meet this definition precisely but have few treatment options.

Innovation

HLC strongly supports policies that are transparent and incentivize innovations that enable all Americans to live longer, healthier lives. We have already seen several biopharmaceutical companies withdraw medicines from clinical trials because of the expectation that IRA's price controls would keep them from recouping their investment. We believe this initial guidance will further compound the IRA's negative effects on continued innovation by setting rules that explicitly devalue existing patents or exclusivities for selected drugs.

Within the guidance, CMS states they intend to consider the length of available patents and exclusivities and may consider adjusting the preliminary price downward if the patents and exclusivities will last for several years. We believe this policy penalizes companies that have secured patent rights even prior to approval by the Food and Drug Administration, particularly for small molecules. Devaluing existing patents and exclusivities will also be damaging for post-approval research and development which many manufacturers invest in for patient safety, as well as finding further indications for their medicines that will aid more patients.²

Thank you for the opportunity to provide comments on the initial guidance for the Medicare Drug Price Negotiation Program. HLC looks forward to engaging with the administration as the regulatory process proceeds. If you have any questions, please do not hesitate to contact Debbie Witchey at (202) 449-3435 or dwitchey@hlc.org.

¹ Medicare Part D: A First Look at Medicare Drug Plans in 2023, Kaiser Family Foundation <https://www.kff.org/medicare/issue-brief/medicare-part-d-a-first-look-at-medicare-drug-plans-in-2023/>

² PhRMA. "[WTAS: Inflation Reduction Act already impacting R&D decisions.](#)" January 17, 2023.

Sincerely,

A handwritten signature in cursive script, reading "Mary R. Grealy". The signature is fluid and elegant, with the first name "Mary" and last name "Grealy" clearly distinguishable.

Mary R. Grealy
President

Healthy Men Inc., is a federally qualified non-profit organization dedicated to the health of men and boys and their families. We, along with over 35 other patient advocacy organizations, are concerned about the current approach CMS is taking to implementation of guidelines for the Medicare Drug Pricing Negotiation Program. We believe that the current approach does not serve patients well and offer several comments, as noted below, for your consideration.

Sincerely

Dr. Salvatore J. Giorgianni
Vice-President and Co-Founder
Healthy Men Inc.
and
Chair-Emeritus and Co-Founder
American Public Health Association
Men's Health Caucus

+++++

Dear Congress/CMS:

As patient representatives, we advocate on behalf of patient interests and interpret how certain policies will positively or negatively affect them. Patients know firsthand the benefits of a strong health care system that provides access to new and groundbreaking treatments. In recent years, we have seen great strides in the treatment of ALS, cancer and Alzheimer's disease that have increased lifespan, slowed the ravage of disease and improved the quality of lives.

Last year, Congress passed significant policies within the Inflation Reduction Act (IRA) focused specifically on patient costs. We were especially pleased by the improvements to Medicare Part D that included adding an out-of-pocket cap, establishing a \$35 limit on monthly insulin costs, and eliminating cost sharing for vaccines. These policies will provide immediate relief to patients. Thank you.

However, other policies around prescription drug prices faced significant debate during the legislative process. Policymakers must keep in mind the unknown long-term impacts on the development of new treatments – especially those for complex and rare diseases – and patients' ability to access those new therapies.

Now it is time for the real work as the Administration begins the lengthy process of implementing IRA's policies. We urge Congress to continue oversight throughout the implementation process and insist that patient voices are heard.

The Medicare Drug Price Negotiation Program contained in the law seeks to establish negotiated rates, or the Maximum Fair Price (MFP), for medications. While focused on reducing drug costs, the unintended negative consequences for drug coverage,

formulary priority, access and further research and development could harm patients. For example, as new prices are determined, payors may favor products on their formularies that have a negotiated price. This could ultimately make other medications more difficult to access as payors encourage use of these negotiated price medications and discourage others. Payors already utilize cost saving measures that negatively impact patients such as restrictive formularies, step therapy and strict prior authorizations. Patients need access to the correct treatments, or they will suffer. The addition of products with artificially lowered prices is likely to create yet another restrictive process for patients.

It is critical that the Administration take patient needs and access to treatments into account when implementing the law. To do that we are committed to regular and open communications with CMS throughout the law's implementation and execution. ***We urge Congress to ensure that regulators at CMS create specific opportunities for patient advocates to participate in the regulatory process.***

Our specific recommendations include:

- **Host regional roundtables to solicit feedback from patients.** We strongly recommend that CMS create a structure similar to that used to implement the Affordable Care Act (ACA) and utilize the CMS regional staff to hold patient-centered roundtable discussions throughout the country to ensure that patients have the opportunity to share their experiences and insights directly with CMS, regardless of their physical location. Providing regional opportunities is particularly important in the patient community where resources may make participation at the federal level more of a challenge than in their state and local communities.
- **Release draft guidance, solicit written comments.** We are pleased that CMS has announced that it will issue draft guidance that seeks public input on key provisions of the MFP program. We hope that the draft guidance includes and seeks feedback on the process, including the methodology CMS uses to determine the MFP. Soliciting written comments from the public is critical.
- **Develop patient-centered criteria.** CMS should also develop, with significant input from patients, patient-centered criteria that must be adhered to as CMS implements the drug pricing provisions. This will ensure patient perspectives are heard and patient needs are prioritized. The ACA required that the Center for Medicare and Medicaid Innovation develop similar criteria.
- **Meaningfully engage patients in determining the MFP for each drug.** Patient advocates can offer both substantial and critical perspectives as CMS considers what a price should be for a specific drug. CMS should create a process through which it will consistently and meaningfully engage with patients determining each drug's price, and ensure they have a say in the outcome.
- **Study the impact of the drug pricing provisions on patients.** CMS should study the impact that negotiation has on patients prior to negotiation, focusing on issues related to access to current and future therapies. For example, CMS

should study the impact of the drug pricing provisions on Medicare Part D coverage, including formulary placement and utilization management.

Should you have any questions or comments, please contact Liz Helms, Founding Director, CCPA at lizh@chroniccarealliance.org. Thank you for your time and attention to these critical issues.

Sincerely,

Chronic Care Policy Alliance (CCPA)

Alliance for Aging Research

ALLvanza

American Behcet's Disease Association (ABDA)

Applied Pharmacy Solutions

Autoimmune Association

Axis Advocacy

Black, Gifted & Whole Foundation

Cancer Support Community

Chronic Disease Coalition

Coalition of Wisconsin Aging and Health Groups

Colorado Gerontological Society

GO2 for Lung Cancer

Healthy Men Inc.

Hereditary Neuropathy Foundation

HIV + Hepatitis Policy Institute

ICAN, International Cancer Advocacy Network

International Foundation for AiArthritis

Lazarex Cancer Foundation

Let's Talk About Change

Looms For Lupus

Men's Health Network

MLD Foundation

National Association of Nutrition and Aging Services Programs (NANASP)

National Hispanic Medical Association

National Patient Advocate Foundation

National Puerto Rican Chamber of Commerce

Neuropathy Action Foundation (NAF)

Nevada Chronic Care Collaborative

Partnership for Innovation and Empowerment

Partnership to Fight Chronic Disease

Patients Rising Now

RetireSafe

Southern Christian Leadership Global Policy Initiative (SCL-GPI)

Support For People With Oral And Head And Neck Cancer, Inc. (SPOHNC)

The National Puerto Rican Chamber of Commerce



April 14, 2023

Meena Seshamani, MD, PhD
Deputy Administrator
Centers for Medicare & Medicaid Services
Hubert H. Humphrey Building
200 Independence Avenue SW
Washington, DC 20201

Re: Comments on *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026*

Dear Dr. Seshamani:

The **HIV+Hepatitis Policy Institute** is a leading national HIV and hepatitis policy organization promoting quality and affordable healthcare for people living with or at risk of HIV, hepatitis, and other serious and chronic health conditions. Given the importance of medications to the health and well-being of people living with and at risk of HIV, people with hepatitis B & C, and their growing reliance on Medicare for prescription drugs, we are keenly interested in the implementation of the *Medicare Drug Price Negotiation Program* that CMS is setting up as required by the *Inflation Reduction Act* (IRA). While much of the request for comments contained in the *Initial Memorandum* are more appropriate for drug manufacturers to respond to, patient groups such as ours are also keenly interested in the negotiation process and its outcomes.

Patients are looking forward to the implementation of the IRA and its new \$2,000 out-of-pocket maximum along with an annual smoothing mechanism. We are also closely monitoring the *Medicare Drug Price Negotiation Program* to ensure that patients will directly benefit from the process in the form of lower out-of-pocket costs and fewer access barriers such as utilization management. We are also concerned about the unintended consequences of the *Negotiation Program*. We want to make sure that as a result of the negotiation process, patient access to the medications they need will not be reduced by more limited formularies and increased utilization management. At the same time, patients should not pay higher out-of-pocket costs for drugs that are not undergoing the negotiation process. Additionally, patients need assurance that the *Negotiation Program* will not impede development of new medications that can help improve the lives and well-being of people not only here in the United States but throughout the world.

HIV+HEPATITIS POLICY INSTITUTE

1602B Belmont Street NW | Washington DC 20009 | 202-462-3042 | 202-365-7725 (cell)

HIVHep.org | Twitter: @HIVHep | Facebook: HIVHep

Our comments below are not in order of importance but follow the order of the *Initial Memorandum*. The **HIV+Hepatitis Policy Institute** has also reviewed the *Information Collection Request for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act* and will separately provide comments on the proposed data collection elements, but our review of this document has also helped inform the comments below.

Sections 50.1 Manufacturer Specific Data & Section 60.3.4 Consideration of Manufacturer Specific Data

The **HIV+Hepatitis Policy Institute** has witnessed the ups and downs of the drug development process over the years. Drugs to treat HIV have progressed from the first antiretrovirals with serious side-effects and limited effectiveness to more effective multi-drug regimens to highly safe and effective single-tablet antiretroviral regimens which enable people with HIV today, not only in the United States but around the world, to live as long as people who do not have HIV. We now even have drugs that prevent HIV as well as new long-acting medications for the treatment and prevention of HIV, with more in the pipeline. Hepatitis B can be treated with daily drugs and Hepatitis C can be *cured* in as little as 8 to 12 weeks. Drug researchers are currently working on a cure for HIV and hepatitis B and vaccines for HIV and hepatitis C.

While CMS is seeking specific data points for the costs and revenues for specific drugs, the research and development process for drugs does not work on an individual drug by drug process. It is essential to look at research and development costs not just for an individual drug, but in the aggregate, including the vast majority of medications in the R&D pipeline that never make it to market. Again, we would expect drug manufacturers to explain all of this in their comments but given our experience in the significant advances in HIV and hepatitis drug development, we are keenly aware of how these advancements have taken place.

By requesting data on specific drug costs and revenues at the time of the negotiation process, CMS is ignoring many factors including the following:

- 1) The years of R&D that the drug manufacturer invested and learned from as it researched other drugs that led to the development of the negotiated drug;
- 2) The failures and costs of those other drugs;
- 3) Manufacturers may highly profit from the negotiated drug in order to invest in other drugs that fail or may not be as profitable;
- 4) The investment and costs that may occur for new indications for the negotiated drug, along with future revenue that may arise from it;
- 5) The investment the manufacturer is making on new drug development that is not associated with the negotiated drug;
- 6) The amount and costs of free or reduced cost drugs the manufacturer provides globally to low income countries; and
- 7) The value of the drug to the rest of the world and eradicating illnesses, such as infectious diseases.

Seeking specific data on only the drug that is subject to negotiation does not fully capture the aggregate cost of drug development and will likely curtail future drug development by undervaluing the R&D process.

Section 60.3.3.1 Analysis for Selected Drugs with Therapeutic Alternatives

This seems to be the only section for which the public, including patient groups, will be able to provide comments on the negotiation process. Not only is the scope very limited, but the comment period will only be 30 days, leaving under-resourced patient groups and the general public out of the process. Since we have reviewed the proposed *Information Collection Request* for this section, we also know that CMS will only be collecting comments that are cited in literature. This is not a true public comment period that patients and their providers can participate in.

We would urge CMS to provide more opportunities for public input into the negotiation process so we can offer true comment on the patient experience and our needs. There are many factors that should be addressed that CMS is not seeking public comment on, including how specific drugs promote health equity and reduce racial, ethnic, and other health disparities. These matters are particularly important to people with or at risk of HIV and hepatitis. CMS must also take into account that not every patient is the same and reacts to a particular drug in the same manner. Further, not everything patient communities would want to comment on is cited in literature.

We urge CMS to provide additional opportunities for meaningful public comment as part of the negotiation process and to offer responses to the comments submitted.

Section 110 Part D Formulary Inclusion of Selected Drugs

The proposed guidance offers just one sentence on the topic of formulary inclusion of drugs selected for the *Negotiation Program*, merely restating what is in the law, namely that a negotiated drug must be covered by Medicare plans. We believe that patients need to realize a substantial benefit for any drug that undergoes the negotiation process. Patients should be able to access the drug at the lowest tier and free of any utilization management barriers such as prior authorization and step therapy. Since the IRA will most likely impact the price of similar drugs, patients should also benefit from their reduced costs and should realize those savings free of restrictions.

While plans are required to cover negotiated drugs, we are concerned at the same time that plans may limit the inclusion of non-negotiated drugs. This would be damaging to the health and well-being of Medicare beneficiaries.

We urge CMS, as it implements the drug negotiation process, to monitor benefit plan design to ensure that access and affordability of Medicare drugs are not diminished.

Thank you for this opportunity to comment on this proposal. Should you have any questions or need any additional information, please do not hesitate to reach out via phone at (202) 462-3042 or email at cschmid@hivhep.org.

Sincerely,

A handwritten signature in blue ink, appearing to read 'Carl E. Schmid II', with a stylized flourish at the end.

Carl E. Schmid II
Executive Director



April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health & Human Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Re: Medicare Drug Price Negotiation Program Guidance: Initial Memorandum, Implementation of Section 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Seshamani:

In response to the Centers for Medicare & Medicaid Services' (CMS) "Drug Price Negotiation Program Guidance: Initial Memorandum, Implementation of Section 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments", Incubate submits the below comments to express our concern that the guidance does not consider industry warning signs and will have a detrimental impact on future investment in the life sciences, ultimately to the detriment of patients.

Incubate is a coalition of early-stage life sciences venture capital firms representing the patient, corporate, and investment communities. Our primary aim is to educate policymakers on the role of venture capital in bringing promising treatments to patients in need.

CMS Doubles Down on Price Controls

Since passage of the Inflation Reduction Act (IRA) in August 2022, Incubate has sounded the alarm that the law creates significant uncertainty for the life sciences investor community and upends the successful ecosystem of biopharmaceutical investment, research, and development that has enabled the United States to lead the world in developing new drugs. A number of investors and companies have already shifted resources away from developing small molecule medicines and pursuing post-approval research in light of the IRA.¹

We are disappointed that despite the opportunity to correct the law's ambiguity, CMS' initial implementation guidance lacks transparency in the price setting process and does not address fundamental issues created by the law.

Lacks Transparency in the Price Setting Process

In this guidance, CMS did not address the significant confusion with the implementation of the law in a way that would protect incentives towards innovation. The Agency did not consider mitigating the law's impact and, in fact, doubled down on problematic components of this law.

¹ Incubate Coalition. (n.d.). Life Science Investment Tracker. Retrieved April 14, 2023, from <https://incubatecoalition.org/life-science-investment-tracker/>

One example is CMS' very broad interpretation of what forms of a drug should qualify for price setting. CMS is choosing to apply the maximum fair price (MFP) to all forms of a drug with the same active ingredient or active moiety, even if they are completely new forms (e.g., IV vs. subcutaneous), approved under different product applications at the FDA, and regardless of whether all the forms meet the age requirement for an eligible drug. Investors continue to be concerned about the broad application of MFP, which will drive less investment and development.

Disincentivizes Small Molecule Drug Development & Post-Approval Research

The guidance also reinforces the IRA's perverse incentive to invest in biologics, instead of the development of small molecules. As we have noted previously, the standard 14-plus year calculation, established by a combination of patents and exclusivities, that venture capitalists rely on to recoup their investments, has shifted under this law to provide a larger reward for the development of biologics (13 years) than the development of small molecules (nine years).² The larger reward for biologics, ensured by the additional four-year exemption from price setting, penalizes small molecule development.

Small molecule drugs offer enormous benefits, both to patients and the health system, especially when they become inexpensive generics. These are not just the pills of yesterday. Small molecule drugs, some of which can cross the blood-brain barrier, offer hope for neurological diseases like Alzheimer's and brain cancer, which was highlighted in President Biden's Cancer Moonshot effort. Understanding the simple economic principle that capital will be allocated in the direction of the biggest risk-adjusted reward, we can anticipate fewer investments in small molecule medicines, which will be detrimental to patients.

We are also concerned that this guidance will discourage drug makers and venture capitalists from pursuing new uses for existing drugs through post-approval or secondary indications. The guidance specifically references how extending patents and exclusivities could directly lower MFP calculations:

“In considering element (4) on patent applications, exclusivities, and applications and approvals for the selected drug, CMS intends to consider the length of the available patents and exclusivities before the selected drug may no longer be single source. For example, if the selected drug has patents and exclusivities that will last for a number of years, CMS may consider adjusting the preliminary price downward.”³

The IRA's price-setting timelines already signaled to drug developers that they not follow the science, as any returns on investment will get cut off before new uses for medicines are developed. Under CMS' guidance, companies will now be penalized for successfully innovating new uses by lowering the preliminary price if there are existing patents and exclusivities on a drug. As a result,

² Stanford, J. March 6. Congress must fix IRA small-molecule penalty. Stat News, <https://www.statnews.com/2023/03/06/congress-must-fix-ira-small-molecule-penalty/>.

³ Centers for Medicare & Medicaid Services. (2021). Medicare Drug Price Negotiation Program: Initial Guidance. Retrieved April 14, 2023, from <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>



we expect research and development efforts towards secondary indications will decrease, thus limiting the investment and exploration of new or alternative applications of medical discoveries - which are critical for continued R&D in sectors like cancer.

Distorted Calculation of the MFP

The investor community is also unsettled about the opacity around the MFP calculation. Under CMS' guidance, there will be no understanding of the justification of the 2026 MFPs until after the next group of drugs are selected for negotiation. Disconcertingly for investors, there is also no visibility into CMS' process for their calculation.

In addition, all of the valuable contributions to raise an MFP are not being taken into account. We ask that the Agency consider the clinical, patient, and societal benefits of a drug when determining the calculation of MFPs. CMS does not currently take these variables into account, despite them significantly contributing to the value of the drug. We urge CMS to allow these variables to increase the MFP.

Perverse Signal to the Market

Finally, I must underscore the most concerning signal that this rule sends to the market: that following the science will not be rewarded moving forward. Our current life sciences ecosystem – one that made the United States the top drug developing nation in the world – has previously operated by pursuing science first. This rule sends a signal to both innovators and investors that some discoveries are more valuable than others, and that some should not be further developed. If not corrected, we are fearful of the long-term ramifications on American biopharmaceutical discovery.

Thank you for your consideration in these comments, please do not hesitate to contact John@incubatecoalition.org for additional information.

Sincerely,

John Stanford
Executive Director
Incubate



Incyte Corporation
1801 Augustine Cut-Off
Wilmington, DE 19803
Tel: 302.498.6700
Web: www.incyte.com

April 14, 2023

SUBMITTED ELECTRONICALLY VIA IRAREbateandNegotiation@cms.hhs.gov

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attn: PO Box 8016

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Dr. Seshamani:

Incyte appreciates the opportunity to submit comments in response to the Centers for Medicare and Medicaid Services' (CMS's) *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (the Guidance).¹

At Incyte, we exist to positively affect the lives of patients through heavy investment in biopharmaceutical R&D. To this end, we employ more than 800 world-class scientists who are committed to finding solutions for some of the most critical unmet medical needs. In 2022 alone, Incyte invested \$1.6 billion on R&D, representing nearly 47% of the company's total net revenues during that time. Revenue from sales of our approved products, chiefly Jakafi® (ruxolitinib), fuel Incyte's clinical development program of 25 investigational medicines intended to transform the treatment of cancer and inflammatory and autoimmune conditions.²

Incyte supports the comments submitted by our trade associations, the Pharmaceutical Research and Manufacturers of America ("PhRMA") and the Biotechnology Innovation Organization ("BIO") on the Initial Guidance. Incyte writes separately to provide our comments on Section 60, specifically in response to CMS's solicitation for comments on section 60.1 "Establishment of a Single Proposed MFP for Negotiation Purposes."

Incyte is concerned that CMS is not accepting comments on the qualifying single source drug (QSSD) definition and other foundational issues in Section 30. Because CMS has issued Section 30 as final without comment solicitation, Incyte is not providing comments on that section; however, as we previously stated in our comment

¹ Available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>

² Incyte Corporation Pharmaceutical Portfolio, <https://www.incyte.com/what-we-do/pharmaceutical-portfolio> (last visited March 6, 2023).

letter on the small biotech ICR, Incyte believes that CMS's expansive interpretation of a QSSD is contrary to the statute, and strongly disagrees with the approach.³

As Incyte has previously communicated with CMS, the core concern at the root of our comments in this letter is that Opzelura™ (ruxolitinib) cream and Jakafi® (ruxolitinib) are different U.S. Food and Drug Administration (FDA)-approved drugs that are indicated to treat entirely different conditions in different therapeutic areas—dermatological vs. antineoplastic indications—with no overlap. Yet, because these two drugs share an active ingredient—if Opzelura and Jakafi were selected under the Drug Price Negotiation Program— CMS proposes to establish a single maximum fair price (MFP) for these two different drugs that are indicated to treat wholly unrelated patient populations with separate and distinct medical conditions (that vary greatly in prevalence). In light of these profound differences, these two drugs compete in separate therapeutic classes with dissimilar marketplace characteristics and as a result—not surprisingly—they have different pricing that bears no relation to one another. As Incyte's comments illustrate, CMS's guidance regarding the establishment of a single proposed MFP at the outset of the negotiation process is unworkable with these two drugs.

Further, we want to bring to CMS's attention the challenges of basing such a price on a 30-day equivalent supply for certain dosage forms, especially for a cream product like Opzelura where an amount used cannot be generalized across patients and a prescriber cannot prescribe the product based on a finite quantity over a particular period of time.

Incyte's comments on the Guidance include the following:

- I. CMS Should Clarify How It Intends to Establish a Single Price for Two Drugs That Have Separate Indications, Compete in Separate Therapeutic Classes, Have Wholly Unrelated Patient Populations, and as a Result Have Different Pricing
- II. CMS Should Clarify How It Intends to Develop an MFP Considering Therapeutic Alternatives for Different Disease States in Different Therapeutic Classes With Different Marketplace Characteristics
- III. CMS's Approach to Apply Ratios for Each Dosage Form and Strength Is Flawed
- IV. CMS Should Clarify How It Intends to Calculate 30-Day Supplies for Topical Medications
- V. CMS Should Clarify How It Intends to Handle Federal Supply Schedule (FSS) and Big Four for Manufacturers that Offer Dual Prices

- I. **CMS Should Clarify How It Intends to Establish a Single Price for Two Drugs That Have Separate Indications, Compete in Separate Therapeutic Classes, Have Wholly Unrelated Patient Populations, and as a Result Have Different Pricing**

As noted, Opzelura and Jakafi are different products that are indicated to treat entirely different conditions in a different therapeutic area—dermatological vs. antineoplastic/immunological indications—with no overlap. Additional differences between the products are included in Table 1. **Given the vast differences between these drugs, including among the statutory factors CMS must consider when establishing the MFP, it is unclear how CMS could establish a single price that is “fair” with respect to both products.**

³ Incyte Comments on the Information Collection Request regarding the Small Biotech Exception, CMS-2023-0008-0001 (Mar. 27, 2023), available at <https://www.regulations.gov/comment/CMS-2023-0008-0002>.

Table 1: Key Differences between Jakafi and Opzelura

Ruxolitinib Phosphate → Active Pharmaceutical Ingredient in two separate drugs marketed by Incyte			
	Jakafi	Overlap	Opzelura
Product Form	Tablet (60 count bottle)	×	Topical Cream (1.5%, 60 gm tube, 100 gm tube)
Route of Administration	1 tablet taken twice a day by mouth	×	Applied thin layer twice daily directly to affected area of skin; up to 20% (atopic dermatitis) or 10% (non-segmental vitiligo) of body surface area
Key Studies	<u>COMFORT-1</u> <u>COMFORT-2</u> <u>RESPONSE</u> <u>REACH-1</u> <u>REACH3</u>	×	<u>TRuE AD1</u> <u>TRuE AD2</u> <u>TRuE-V1</u> <u>TRuE-V2</u>
Uses Addressed by Approved Indications	Antineoplastics Approvals -Myelofibrosis ^{1,2} (2011) -Polycythemia Vera ^{1,2} (2014) Immunological Approvals -Acute Graft Versus Host Disease ^{1,2} (2019) -Chronic Graft Versus Host Disease ^{1,2} (2021)	×	Dermatological Approvals -Mild to Moderate Atopic Dermatitis (2021) -Non-Segmental Vitiligo ¹ (2022)
Wholesale Acquisition Costs	Jakafi's WAC per package (5-25mg/1 (60 tablets)) in 2023 ~\$16,600	×	Opzelura's WAC per package (15mg/g (60g tube)) in 2023 ~\$2,000
Distribution*	Specialty Distributors Specialty Pharmacies	×	Full Line Wholesalers Retail Pharmacies
Standalone Approvals	Each product was approved under a separate, complete NDA reviewed by different, distinct review divisions within the FDA		

1. Approval represents area of unmet need – first approved therapy for indication

2. Rare Disease

*As of the date of this comment letter

Given the degree of differences between Jakafi and Opzelura, we believe that applying a single MFP across these products is misguided. Assuming these two drugs are part of the same negotiation—which we strongly disagree with because Opzelura is not a new formulation of Jakafi—then we recommend that CMS arrive at a single MFP (using ratios or some other equitable means) towards the end of the negotiation, not the start.

II. CMS Should Clarify How It Intends to Develop an MFP Considering Therapeutic Alternatives for Different Disease States in Different Therapeutic Classes With Different Marketplace Characteristics

As discussed in Section IV, because a 30-day supply of Opzelura can vary greatly from patient-to-patient -- or even for a given patient depending on their symptoms during that time -- we do not understand how CMS will determine the 30-day supply. Even assuming CMS could develop a reasonable proxy for a 30-day supply, combining non-FAMPs and Part D net prices for products with such vastly different pricing results in a ceiling that bears no resemblance to these pricing metrics for the particular products. (For example, as described further below, Non-FAMP for Jakafi is approximately 8x greater than that of Opzelura).

Based on the statutory negotiation factors related to “therapeutic alternatives” listed at SSA 1194(e)(2), it is unclear how CMS will establish a starting point for, and make adjustments to, the initial offer price when such factors are totally unrelated and significantly different.

To develop a “preliminary price” for the Initial Offer, CMS intends to identify therapeutic alternative(s) of the QSSD, consider the therapeutic alternative(s)’ Part D net price or Part B ASP, as applicable, and evaluate the clinical benefit of the QSSD compared to its therapeutic alternative(s) for each of the QSSD’s indications. If there are multiple therapeutic alternatives, CMS intends to consider the range of net prices and/or ASPs as well as the utilization of each therapeutic alternative to determine the starting point within that range. CMS will then adjust the preliminary price based on other manufacturer-specific data, submitted under SSA 1192(e)(1).

Once the starting point for the initial offer has been established, CMS proposes to adjust the starting price by evaluating the clinical benefit conferred by the selected drug compared to its therapeutic alternatives and then consider each category of the manufacturer-specific data. Incyte requests that CMS provide clarity on how the Agency intends to consider these criteria and establish a single MFP for a cancer therapy and a dermatological cream. How will CMS account for the differences between these products when compared to their therapeutic alternatives? How will CMS weigh manufacturer-specific data that varies significantly across these two drugs? For example, in circumstances where a factor with respect to one drug counsels for a downward adjustment while the same factor with respect to the other drug counsels for an upward adjustment, how will CMS determine the impact of that factor?

III. CMS’s Approach to Apply Ratios for Each Dosage Form and Strength Is Flawed

After CMS establishes a single MFP, the Agency intends to convert that single MFP into per-unit MFPs for each different dosage form and strength of a QSSD. While Incyte agrees that the approach to negotiate a single price across all dosage forms and strengths is one permissible interpretation of the statutory requirements at 1194(c)(1)(A), we do not believe this process is the only permissible interpretation, and it is not appropriate for products like Jakafi and Opzelura.

If CMS were to move forward and apply these MFP ratios at the NDC level for products such as Jakafi and Opzelura, it would further exacerbate the flawed process outlined in Section II. At issue is the fact that CMS will select a single MFP and then scale it to each of the QSSD’s different dosage forms and strengths. Applying this WAC price ratio at the end does not cure the flawed process to establish the single MFP in the first place. Further, we believe it may penalize more expensive dosage forms and strengths of the QSSD. Jakafi’s WAC per package in 2023 is approximately \$16,600 whereas Opzelura’s WAC per package in 2023 is approximately \$2,000. As of today, this 8x pricing metric extends roughly to comparisons of the products’ AMPs, NFAMPs, Federal Supply Schedule (FSS), and Other Government Agencies (OGA) prices. Since CMS scales the NDC-specific MFP only after considering the products together at all of the earlier stages, the underlying MFP is likely to have significant challenges given that it was developed in a way that attempts to consider and reconcile various inputs across two drugs that are wholly unrelated to each other.

Incyte believes that CMS’s current intended approach that would allow products like Jakafi and Opzelura to be part of the same negotiation is flawed because CMS consolidates various pricing and other data of entirely unrelated products to produce a single “fair” price. The ratios applied to each NDC will likely have significant problems given that it would be developed in a way that attempts to consider and reconcile various inputs across products that are wholly unrelated to each other.

There is a path for CMS to remedy the complex challenges that drug products like Jakafi and Opzelura present, even with their differing indications, routes of administration, and therapeutic alternatives. For cases like Incyte’s, CMS should reserve to itself the option to “split” the negotiation into two tracks, and separately consider the merits of each drug at certain points during the process. This can be performed in a manner consistent with CMS’s current interpretation of IRA’s mandate to aggregate drug products into a single QSSD, and negotiate a “single” MFP. For example, at the outset of the process, Jakafi and Opzelura would be treated as a single QSSD for

purposes of selection and calculation of total Medicare expenditures. Yet from there, CMS could calculate a ceiling price, starting point and initial offer for the two drugs separately. The negotiation process would yield two MFP-component prices, one for each drug, which CMS could then blend into a single MFP based on the relative weights of the two drugs' WACs. That single MFP would satisfy the requirement of SSA 1194(c)(1)(A). Finally, CMS could disaggregate that single MFP, again on the basis of WAC, to re-create the two MFP component prices negotiated for the two different drugs.

IV. CMS Should Clarify How It Intends to Calculate a 30-Day Supply for Topical Medications

CMS intends to establish a ceiling and the MFP based on a 30-day equivalent supply of a selected drug. However, there will be significant challenges creating a 30-day supply amount for topical medications, such as creams, foams and ointments. Based on the initial guidance, it is unclear how CMS will develop a 30-day supply for a topical drug like Opzelura, the amount of which depends on the size of the affected area for a patient. For patients using Opzelura to treat atopic dermatitis, the Prescribing Information directs them to "[a]pply a thin layer twice daily to affected areas of up to 20% body surface area."⁴ For patients using Opzelura to treat nonsegmental vitiligo, the Prescribing Information directs the patient to apply "[a]pply a thin layer twice daily to affected areas of up to 10% body surface area."⁵ Thus, the amount of product actually used by patients on a 30-day-basis can vary significantly, both from patient-to-patient as well as for a given patient depending on their symptoms at the time. With this variability, forecasting an annual number of refills in order to estimate a 30-day supply price estimate will likely lead to inaccurate results further complicating and calling into question CMS's intended single-MFP approach.

Incyte requests that CMS issue guidance clarifying how CMS intends to calculate a 30-day supply for topical medications.

V. CMS Should Clarify How It Intends to Handle Federal Supply Schedule (FSS) and "Big Four" Pricing for Manufacturers that Offer Dual Prices

CMS states that "if there is a single therapeutic alternative with a price above the statutory ceiling, then CMS intends to determine the starting point for the initial offer based on the [FSS] or [Big Four] price."⁶ CMS also intends to collect information on the QSSD's FSS and Big Four prices for purposes of adjusting the initial offer price.⁷

The VA guidelines permit manufacturers to choose either single or dual pricing for its covered drugs.⁸ Under the single pricing scenario, manufacturers sell each covered drug to all FSS customers (Big Four and Other Government Agencies (OGA) at one price that is at or below the federal ceiling price. On the other hand, under the dual pricing scenario, manufacturers have two prices for each covered drug, which include (1) an FSS price for the Big Four federal agencies that does not exceed the federal ceiling price; and (2) an FSS price for all OGAs that is not limited to the federal ceiling price.

CMS should clarify how it intends to use the "FSS or Big Four" prices for purposes of setting and/or adjusting the initial offer price. There are instances where a manufacturer elects to offer different FSS prices to "Big Four" agencies as compared to OGA customers. Based on the Initial Guidance, it is unclear how CMS would take that split pricing into account in terms of setting the initial offer price and/or modifying it. Incyte recommends that

⁴ Opzelura Prescribing Information, section 2.2 available at <https://www.opzelura.com/prescribing-information.pdf>.

⁵ Opzelura Prescribing Information, section 2.3 available at <https://www.opzelura.com/prescribing-information.pdf>.

⁶ See Section 60.3.2, at 49.

⁷ See Guidance, p. 89.

⁸ See VA Dear Manufacturer Letter (May 4, 1993).

CMS clarify how it intends to use Federal Supply Schedule pricing when different pricing exists for Big Four and OGA agencies.

Incyte appreciates the opportunity to comment on this Memorandum. We hope that CMS will provide clarity on the issues outlined above. We would welcome the opportunity to meet with you or answer any questions CMS may have about our comments, at your request. Thank you.

Sincerely,

A handwritten signature in cursive script, reading "Barry Flannery".

Barry Flannery
Executive Vice President & General Manager
North America

April 13, 2023

Dr. Meena Seshamani, M.D., Ph.D.

Director, Center for Medicare

Centers for Medicare and Medicaid Services

Department of Health and Human Services

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026

Dear Dr. Meena Seshamani, M.D., Ph.D.,

Thank you for the opportunity to comment on the initial guidance regarding implementation of sections 11001 and 11002 of the Inflation Reduction Act (IRA) (P.L. 117-169), which establish the Medicare Drug Price Negotiation Program to negotiate maximum fair prices for certain high expenditure, single source drugs and biological products.

My comments on this initial guidance are reflective of my experiences as a Health Economist in the pharmaceutical industry generating and leveraging evidence for Health Technology Assessments and drug price negotiations with government payers, primarily outside of the United States. I am also a Doctoral student in Health Policy at Johns Hopkins Bloomberg School of Public Health. The comments I have provided below are my own and do not reflect the opinions of any organizations that I am affiliated with other than myself.

In the final guidance for implementing the Medicare Drug Price Negotiation Program it is critical that CMS provide more clarity regarding the negotiation factors included in section 50. The initial guidance does not currently include the specificity necessary to ensure that the appropriate evidence is generated, provided and reviewed to inform maximum fair price negotiations.

The following comments are specifically referring to Section 50.2, *“Evidence About Therapeutic Alternatives for the Selected Drug”*. This section states that CMS will consider, “The extent to which the selected drug represents a therapeutic advance compared to existing therapeutic alternatives for the selected drug and the costs of such existing therapeutic alternatives”. My first comment refers to the statement, “The extent to which the selected drug represents a therapeutic advance”. My second comment refers to the statement, “compared to existing therapeutic alternatives”. My third comment refers to comparing the costs of selected drugs with, “the costs of such existing therapeutic alternatives”.

My first comment on section 50.2 is referring to the statement that CMS will consider, “The extent to which the selected drug represents a therapeutic advance”. The definition of a “therapeutic advance” must be explicitly stated in the guidance. A drug can be considered a “therapeutic advance” for a variety of reasons, which may differ by therapy area. Common attributes associated with “therapeutic advances” include improvements in clinical endpoints, improvements in a patient's quality of life and ability to do daily activities, and a reduction in adverse events associated with currently available therapies.

Dr. Aris Angelis and Dr. Panos Kanavos have identified several attributes generally taken into consideration by payers, clinicians and patients when assessing the value of a medicine in their publication, [“Multiple Criteria Decision Analysis \(MCDA\) for evaluating new medicines in Health Technology Assessment and beyond: The Advance Value Framework.”](#) The attributes highlighted include burden of disease (severity, prevalence, availability of treatments), therapeutic impact (clinical endpoints and quality of life), safety (adverse events, tolerability and contraindications), innovation (nature of treatment and ease of use), and societal impact (improving public health, improving productivity, reducing other healthcare costs).

Some of these attributes may not be appropriate for the Medicare Drug Price Negotiation Program given the program will be focusing on single source drugs that have been approved for at least 7 years or biological products that have been approved for at least 11 years. Additionally a societal perspective may not be appropriate for Medicare given the intention of the Drug Price Negotiation Program is to lower the price of some of the costliest single-source brand-name Medicare Part B and Part D drugs. Therefore, the attributes that CMS should consider when defining a “therapeutic advance” should at minimum include burden of disease, therapeutic impact and safety.

My second comment on section 50.2 is referring to the statement that CMS will consider the extent of the therapeutic advance of a drug, “compared to existing therapeutic alternatives”. This statement requires clarification regarding how many “existing therapeutic alternatives” the drug will be compared to and how the appropriate “therapeutic alternative” will be determined.

Dr. Ziouani, Dr. Granados and Dr. Borget assessed the most common approaches to defining comparators for health technology assessments in their publication, [“How To Select The Best Comparator? An International Economic Evaluation Guidelines Comparison”](#). It was determined that the most common approach to selecting a comparator is to use the standard of care for local practice. Given the potential ambiguity of this conclusion, CMS should identify the “existing therapeutic alternative” by assessing the most commonly used alternative to the drug of interest for a specific indication using internal data.

It is also critical to specify how this comparison will be conducted and if there is a preference for clinical trial data, real world data or indirect treatment comparisons. Given the interest in the Medicare population specifically, real world data may be the most appropriate source of evidence for comparing selected drugs with existing therapeutic alternatives.

My third comment on section 50.2 is referring to the statement that CMS will compare the costs of selected drugs with, “the costs of such existing therapeutic alternatives”. This statement requires clarification on the costs that will be considered. Given the focus of the program is to lower the price of some of the costliest single-source brand-name Medicare Part B and Part D drugs, the focus should be on acquisition cost. However, this must be clearly stated in the guidance.

In conclusion, section 50.2 of the final guidance should include the following clarifications:

- A therapeutic advance is defined as a reduction in burden of disease, a significant improvement in clinical endpoints or an improved safety profile compared to standard of care.
- An existing therapeutic alternative is the most commonly used alternative to the selected drug of interest for a specific indication, which will be identified by CMS using internal data.

- The only costs that will be considered are drug acquisition costs. Indirect costs associated with a drug will not be considered.

Thank you again for the opportunity to comment on the initial guidance for implementing the Medicare Drug Price Negotiation Program. If there are any questions regarding my recommendations please do not hesitate to contact me via email at [REDACTED].

Sincerely,

[REDACTED]

[REDACTED] [REDACTED]

Dear Centers for Medicare and Medicaid Services,

Average drug prices are excessive in the USA.

They are much higher than in other developed countries. The average prices of these other developed countries would be a fairer starting point in negotiations. Big Pharmaceutical companies have a long history of callous price gouging.

Thank you

██████ ██████

April 13, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Dear Director Seshamani:

I am writing in response to your March 15 Memorandum on Medicare's Drug Price Negotiation Program, which provides initial guidance on the implementation of sections 11001 and 11002 of the Inflation Reduction Act. Thank you for the opportunity to provide input on this matter.

By way of background, I am a hematologist and the Chief Innovation Officer at Mayo Clinic in Arizona. My work focuses on the treatment of myeloma and related conditions, the genetics of myeloma and related conditions, and the development of novel therapies. I also work in pharmacoeconomics and policy. My comments here should be taken as personal opinion and do not necessarily reflect the thoughts of Mayo Clinic. I have published extensively in the matters I discuss below (Google Scholar April 11th 2023 H Index 125, 60,420 citations)

I am worried about how CMS's new guidance will impact patients living with cancer diagnoses such as multiple myeloma, and other serious illnesses. The guidance seems to double down on shortcomings present within the Inflation Reduction Act, reinforcing policies that will inevitably hinder biopharmaceutical advancement and stifle innovation. I have seen concerning signs that the future development of certain small-molecule medicines may be in jeopardy because of the IRA. I have witnessed conversations on how additional research will not be further supported as a consequence of the IRA provisions.

Consider that CMS's guidance discourages critical "follow-on" innovation, the important research that takes place after a drug is first approved. The guidance suggests that the government will essentially penalize companies that patent novel discoveries made after a medicine is approved, even if those discoveries necessitated years of expensive and risky research.

Scientists regularly conduct research and development long after a medicine has received regulatory approval. This research can help uncover additional benefits for patients. For example, follow-on research can reveal that a medicine approved to treat a disease in a specific phase can also treat the same disease in other phases. Other times, scientists discover that a drug intended for one illness can treat one or more entirely different conditions.

In addition to revealing new uses, follow-on research can also lead to improvements in a drug's safety, efficacy, or method of administration. Many times, post-approval research helps bolster patient adherence, thereby improving clinical outcomes.

Every single drug used for the treatment of myeloma has undergone modifications to its use because of follow-on research. I can provide multiple examples of how follow-on research has helped patients with myeloma and related conditions. Rigorous post-approval clinical trials allow physicians like me to help as many people as possible with the treatments we have available to us.

Severely reducing the length of time drug makers have to charge a market price for their product will make it significantly harder for companies to justify the cost and risk of post-approval research.

A [2022 report](#) from the Food and Drug Administration highlighted 25 particularly meaningful approvals for new uses or indications of approved drugs. Many of these post-approval research breakthroughs provided much-needed treatment options for patient groups with unmet needs.

Consider just two of these new approvals: A groundbreaking treatment for pediatric patients with juvenile myelomonocytic leukemia, a rare blood cancer primarily affecting young children; and two therapies approved for combined use to treat pediatric patients with tumors expressing a BRAF mutation.

Policymakers should focus on protecting and even increasing incentives for post-approval advances, not weakening them. Unfortunately, the new guidance suggests that CMS actions will stifle follow-on innovation continues in the future.

I am also concerned about the Inflation Reduction Act's unequal treatment of conventional, "small-molecule" medications and large-molecule "biologic" treatments. The law subjects new small-molecule drugs to price negotiations after just nine years, while biologic medications are exempt from negotiations for thirteen years following regulatory approval. This will inevitably steer investment dollars away from important small-molecule research.

As a physician familiar with the applications of both small-molecule biologic therapies, I can assure you that penalizing small-molecule development has no basis in science.

For one, small-molecule medications can usually be taken in pill form in the comfort of one's home. This enables individuals to bypass the time and costs associated with visiting hospitals or clinics, where biologic medicines often have to be administered under the supervision of trained professionals. The fact that small-molecules are easier to administer makes them valuable options for rural, economically disadvantaged, and minority populations.

Small-molecules are on the cutting-edge of cancer treatment. Many of the newest, most exciting precision cancer treatments employ small-molecule medications to directly target cancerous cells. Unlike conventional chemotherapy, small-molecule drugs are able to target particular proteins or genes *within* cancer cells, avoiding harmful spillover into normal, healthy cells. This can mean fewer side effects for patients.

Lastly, CMS's new guidance appears to adopt the Inflation Reduction's Act shortsighted focus on drug prices, rather than value and patient outcomes. Since becoming a physician, I've seen, first-hand, how new therapies have transformed the prognosis for myeloma. Thirty years ago, patients with myeloma survived for a median of two years following diagnosis. As of today, the average myeloma patient could expect to live for more than eight years after diagnosis, assuming he or she has access to the best available therapies. Thanks to the revolutionary therapies available today, I firmly believe some patients can be cured of the disease. More on this can be found in "[Value and Cost of Myeloma Therapy—We Can Afford It](#)," a 2018 paper I authored for the American Society of Clinical Oncology's Educational Book. One particularly illuminating finding is that more widely covering the "maintenance drugs" needed to manage chronic illnesses results in substantial net health savings due to reduced hospitalizations, surgeries, and other complications.

A narrow focus on drug prices ignores the reality that biopharmaceutical innovation has been responsible for substantial improvements in our ability to treat myeloma and other cancers. Discouraging future medical progress, as the Inflation Reduction Act will do, is a heartbreaking move in precisely the wrong direction.

The United States is the cauldron of biopharmaceutical progress, with more drugs developed here than the rest of the world combined. The innovative work done in the United States ultimately becomes a gift to all of humanity. Misguided changes to America's regulatory environment will diminish these global benefits considerably. We should all be proud of this contribution.

As Dr. Peter Kolchinsky has rightly stated in his book *The Great American Drug Deal*, society should not think about funding drug development as paying rent forever, but rather as paying off a mortgage in order to be free from debilitating illnesses in the future.

These are just some of my concerns. Without a more rigorous attempt to lessen the negative consequences of the Inflation Reduction Act, the impacts on future biopharmaceutical innovation -- and thus, patient health -- could be catastrophic. Should you have any questions or want to discuss my concerns in further detail, please do not hesitate to contact me.

Sincerely,

Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

RE: Medicare Drug Price Negotiation Program Guidance

To Whom It May Concern:

I am pleased to offer comments regarding the initial memorandum, dated March 15, 2023, regarding implementation of Sections 1191-1198 of the Social Security Act for initial price applicability year 2026. I will focus my comments on Section 50.2 of the memorandum, and specifically CMS' proposals regarding use of comparative effectiveness research and the quality-adjusted life year (QALY) metric.

As the mother of a child with a disability, advocate for the needs of those with disabilities, and former member of the National Council on Disability, I am concerned that CMS' position in the initial memorandum may disadvantage individuals with disabilities. As I outline in greater detail below, I believe CMS' constrained view of the prohibition on the use of QALYs is at odds with the consensus of the disability community, contradicts prior Departmental practice, and could allow for violations of federal law.

The Disability Community Opposes "QALYs and Related Measures"

The drug negotiation regime included in Section 11001 of the Inflation Reduction Act (IRA) had its roots in prior legislation introduced in the House of Representatives in the fall of 2019 as H.R. 3, the Elijah Cummings Lower Drug Costs Now Act. Title I of that bill as introduced created a negotiation process that linked the maximum fair price to the average price of a pharmaceutical in six countries: Australia, Canada, France, Germany, Japan, and the United Kingdom.¹

In response, the Consortium of Citizens with Disabilities (CCD)—the largest coalition of organizations that advocates on disability policy—sent a letter to congressional leaders objecting to the linking of the maximum fair price to international prices. The letter noted that “many of the nations used to create the average international market price rely on QALYs to determine their coverage and prices. CCD is very concerned that these provisions effectively import a QALY-based and discriminatory system from abroad. These systems are discriminatory against people with disabilities and do not have a place in the United States health care system.”²

¹ Proposed Section 1191(c)(3) of the Social Security Act, as included in Section 101(a) of H.R. 3 (116th Congress), the Elijah Cummings Lower Drug Costs Now Act, as introduced, September 19, 2019.

² Letter from Consortium of Citizens with Disabilities to House Energy and Commerce Committee Chairman Frank Pallone, House Ways and Means Committee Chairman Richard Neal, and House Education and Labor Committee Chairman Bobby Scott regarding H.R. 3 (116th Congress), September 24, 2019, <https://www.c-c-d.org/fichiers/CCD-Letter-HR-3-Final-9.24.19.pdf>.

The CCD letter also stated the broader concerns with QALYs among most members of the disability advocacy community:

CCD has expressed concern with the use of value assessments and cost-effectiveness measures that rely on Quality-Adjusted Life Years (QALY). The QALY is a discriminatory measure based on the idea that disabled lives are less valuable than non-disabled lives. CCD opposes the use of QALYs and related measures and supports an explicit ban on the use of QALYs in any health care legislation that considers value or effectiveness of health care.³

Following the CCD letter, the House of Representatives passed in December 2019 a revised version of H.R. 3 that incorporated provisions regarding individuals with disabilities. Specifically, the House bill included language requiring CMS to consider during the negotiating process “information on comparative effectiveness analysis for such products, taking into consideration the effects of such products on specific populations, such as individuals with disabilities, the elderly, terminally ill, children, and other patient populations”—language that largely mirrors Section 1194(e)(2)(C) of the Social Security Act, as enacted by Section 11001 of the IRA.⁴

The 2019 bill passed by the House also included language stating that “the Secretary shall not use evidence or findings from comparative clinical effectiveness research in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, non-disabled, or not terminally ill”—language that also largely mirrors Section 1194(e)(2) of the Act, as enacted by the IRA.⁵

However, the House-passed bill also stated that “nothing in the previous sentence shall affect the application or consideration of an AIM [average international market] price for a selected drug.” In addition, the bill did not include the explicit ban on QALY usage requested in the CCD letter of September 24, 2019.⁶

CMS’ Interpretation Could Allow for Use of the QALY Metric

In Section 50.2 of the initial memorandum, CMS wrote that:

Section 1194(e)(2) of the Act additionally requires that CMS not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

³ Ibid.

⁴ Proposed Section 1194(d)(2)(C) of the Social Security Act, as included in Section 101(a) of H.R. 3 (116th Congress), Elijah Cummings Lower Drug Costs Now Act, as passed by the House of Representatives, December 12, 2019.

⁵ Proposed Section 1194(d)(2) of the Social Security Act, as included in Section 101(a) of H.R. 3 (116th Congress), as passed by the House of Representatives.

⁶ Ibid.

Information submitted by members of the public, including manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested parties, or other information found by CMS that treats extending the life of individuals in these populations as of lower value, for example certain uses of quality-adjusted life-years (QALYs), will not be used in the negotiation process. In instances where a study uses QALYs in a life-extension context but has clearly separated this use of QALYs from other evidence in the report (e.g., clinical effectiveness, risks, harms, etc.) that is relevant to the factors listed in section 1194(e)(2) of the Act, CMS intends to consider such separate evidence. CMS will ask entities submitting information to indicate whether or not their submission contains information from studies that use QALYs in a life-extension context. CMS is soliciting comment on other metrics, in addition to QALYs, that may treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill and that CMS should also exclude from consideration when developing offers and reviewing counteroffers.

In Section 50.2, CMS has echoed Section 1194(e)(2) of the Act regarding the value of extending the life of individuals who are elderly, disabled, or terminally ill. This language also mirrors Section 1182(c)(1) of the Social Security Act, which prohibits the Secretary from using comparative effectiveness research to “determine[e] coverage, reimbursement, or incentive programs under Title XVIII in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, non-disabled, or not terminally ill.”⁷

However, prohibiting the use of QALYs solely “in a life-extension context,” as CMS proposes in Section 50.2 of the memorandum, would permit their use in other contexts—for instance, where a pharmaceutical could improve the quality (as opposed to the quantity) of life for individuals with disabilities, the elderly, or the terminally ill.

Using QALYs in these other contexts would represent bad policy for CMS to pursue, as the QALY metric by definition views the quality of life for individuals with disabilities as of “lesser” value than those without disabilities. More importantly, use of the discriminatory QALY metric can violate other federal laws, even outside of considerations centered on “a life-extension context,” as the initial memorandum proposes.

CMS’ Current Interpretation of Discriminatory Behavior Contradicts HHS’ Prior Actions

The language of Section 50.2 focuses solely on the interactions between QALYs and Section 1194(e)(2) of the Social Security Act. This interpretation would confine any restrictions on QALYs solely to the “life-extension context.” However, CMS’ umbrella department has previously taken a more expansive—and appropriate—view regarding discrimination

⁷ Section 1182(c)(1) of the Social Security Act, as enacted by Section 6301(c) of the Patient Protection and Affordable Care Act, P.L. 110-148.

against individuals with disabilities, a view that CMS should adopt regarding the use of QALYs and similar metrics.

In August 1992, the Department of Health and Human Services (HHS) rejected a Medicaid waiver application from the state of Oregon. HHS denied the waiver because Oregon's rankings for determining services the Medicaid program would cover under the waiver were based "in substantial part on the premise that the life of a person with disability is less than the value of the life of a person without a disability," which in the Department's view violated the Americans with Disabilities Act.⁸

In a letter to Oregon Governor Barbara Roberts explaining the reasons for the rejection, HHS cited several concerning aspects of the ranking mechanism. It viewed a telephone survey used to solicit public opinion regarding the benefits that Medicaid should cover as perpetuating stereotypes against individuals with disabilities.⁹ It also criticized the "community values" section of the rankings—which included metrics like "quality of life" and functional "independence"—as valuing the life of individuals with disabilities less highly than individuals without disabilities.¹⁰ Finally, HHS criticized specific benefit exclusions as discriminatory, such as prohibiting coverage of liver transplants for cirrhosis of the liver associated with alcoholism (but not other conditions), and prohibiting life support for low birthweight babies under 23 weeks' gestation.¹¹

In publicly defending his decision to reject the Oregon waiver, then-Secretary Louis Sullivan stated that "our principal concern is that Oregon's plan in substantial part values the life of a person with a disability less than the life of a person without a disability. This premise is discriminatory and inconsistent with the Americans with Disabilities Act."¹² Oregon subsequently resubmitted the waiver, which HHS approved in March 1993. Oregon's revised waiver deleted language in the original proposal that "weighed the contribution of the services, if any, to a patient's quality of life," in large part due to the objections that HHS had raised regarding its discriminatory nature.¹³

The record regarding the Oregon waiver confirms that HHS has taken action against measures that discriminate against individuals with disabilities, for reasons going far beyond the comparatively narrow "life-extension context" laid out in Section 50.2 of the initial memorandum. CMS should therefore ensure that the data and metrics used in its negotiation process comply not just with Sections 1194(e)(2) and 1182(c) of the Social

⁸ Letter from Health and Human Services Secretary Louis Sullivan to Oregon Governor Barbara Roberts, reprinted in "ADA Analyses of the Oregon Health Plan," *Issues in Law and Medicine* March 1994, <https://law-journals-books.vlex.com/vid/ada-analyses-oregon-health-care-plan-53364177>.

⁹ Ibid.

¹⁰ Ibid.

¹¹ Ibid.

¹² Louis Sullivan, "Oregon Health Plan Is Unfair to the Disabled," *New York Times* September 1, 1992, <https://www.nytimes.com/1992/09/01/opinion/l-oregon-health-plan-is-unfair-to-the-disabled-659492.html>.

¹³ Robert Pear, "White House Expected to Back Oregon's Health Care Rationing," *New York Times* March 18, 1993, <https://www.nytimes.com/1993/03/18/us/white-house-expected-to-back-oregon-s-health-care-rationing.html?module=inline>.

Security Act, but the Americans with Disabilities Act and other measures intended to prevent discrimination against individuals with disabilities.

CMS Should Exclude All Uses of QALYs and Similarly Discriminatory Measures

In 2019, the National Council on Disability (NCD), on which I served, issued a report regarding the use of QALYs. The report “found sufficient evidence of the discriminatory effects of QALYs to warrant concern, including concerns raised by bioethicists, patient rights groups, and disability rights advocates about the limited access to lifesaving medications for chronic illnesses in countries where QALYs are frequently used.”¹⁴

The examples compiled in the NCD report explain why the Consortium of Citizens with Disabilities has stated it “opposes the use of QALYs and related measures.”¹⁵ Related measures would include metrics like the equal-value of life year gained (evLYG), which discriminates based upon age and contains similar flaws regarding quality-of-life improvements.

To protect against any discrimination against the most vulnerable in society, CMS should utilize a less constrained interpretation of factors and evidence it will exclude from the negotiation process than that spelled out in Section 50.2 of the initial memorandum. Specifically, CMS should exclude any data or findings that use quality-adjusted life years, or other similar metrics like the equal-value of life year gained, from the negotiation process.

¹⁴ National Council on Disability, “Quality-Adjusted Life Years and the Devaluation of Life with Disability,” Bioethics and Disability Series, November 6, 2019, https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf.

¹⁵ CCD Letter to Chairmen Pallone, Neal, and Scott.

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Inflation Reduction Act (IRA) Initial Program Guidance; Comment Request CMS-1800-NC2

Comment On: CMS-2023-0065-0001

Guidance: Inflation Reduction Act Initial Program

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Comment on CMS_FRDOC_0001-3516

Submitter Information

Name: [REDACTED]

Address:

Email:

Phone:

General Comment

The negotiation of drug prices will be a long-awaited benefit for seniors on Medicare.

As a Medicare Ship Counselor, I find that my clients become most frustrated with the following:

1. Manufacturers make drug price changes after annual enrollment. The beneficiary has selected and enrolled for the following year with no guarantee of the price they will pay.
2. Lack of education on how the pricing works. The contracting with Manufacture, Insurance, and Pharmacies. Posting the negotiated rate with NOC and at the Pharmacy may be helpful.
3. Shopping for the best price is difficult when the pharmacy says I need the script. Many times the scripts are sent electronically to one pharmacy. More upfront transparency is needed on prices.

Hello.

In response to CMS's request for comment by April 14, 2023 at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf> (at page 1), I strongly support any efforts that allow the federal government to negotiate Medicare Part D prices with manufacturers, providers, and suppliers (including pharmacies) that furnish Medicare Part D drugs. In my view, the lack of such negotiating power in the historic Medicare Part D legislation signed into law by President George W. Bush was a major failure and only highlighted the immense power of the Big Pharma lobbyists and political money.

It is my fervent hope that President Joseph R. Biden, Jr. will quickly (preferably before 2026, which is the target date set forth in the guidance for the initial negotiations) and effectively correct this colossal mistake for the financial—and, most importantly, clinical—benefit of tens of millions of Medicare enrollees. The general welfare, which includes true access to the medications they need, of our elderly and disabled population should be a much higher priority and consideration than any political funding concerns. I do not believe that the ability of the Medicare program to negotiate drug prices, as every other health care insurer in the U.S. already does, will significantly impact the research and development of important new drugs despite Big Pharma's contrary and entirely self-serving arguments. My only concern is that the Negotiation Program does not go far or fast enough.

Should you have any questions or need more information about my support for the Negotiation Program, you may contact me at this email address or [REDACTED]. Thank you.

Sincerely, _____
[REDACTED]



11025 N. Torrey Pines Rd
Suite 200
La Jolla, CA 92037

April 10, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Inhibrx appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

While Inhibrx is developing biologic therapeutics for oncology and orphan indications, we strongly believe small molecule drugs will see a significant decrease in investor funding based on the changes in the IRA impacting the 9-13 year period. Prior to founding Inhibrx in 2010, I was the principal of a biotechnology investment fund for 8 Years. During that time my fund did extensive analysis of the costs, success rates and commercial revenues from small molecule drugs and we concluded that investor returns across small molecule programs were at best low single digits and likely barely breakeven. With the impact of the 9-13 year period small molecule drug development is no longer economically viable.

We also believe there are small molecule programs in development that will choose only one orphan disease to pursue when the therapeutic could have benefit across several orphan diseases. We are fortunate that biologics managed to retain 13 years of market-based pricing before having their price impacted by Medicare negotiation which also spills over into Medicaid; we urge CMS reduce the prices of small molecule drugs during the 9-13 year period only as little as required by IRA. Wherever it may be possible to interpret the IRA in such a way as to exempt a small molecule from the IRA, we hope CMS will.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors as well as those with orphan diseases from fewer innovative medicines is minimized. Please contact Mark Lappe, CEO of Inhibrx, by telephone at (858)759-1499 or by e-mail at mark@inhibrx.com, if you have any questions regarding our comments.

Sincerely,

Mark Lappe



April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Dear Dr. Seshamani,

The Innovation and Value Initiative (IVI) appreciates the opportunity to provide comments to the Centers for Medicare and Medicaid Services (CMS) on the initial guidance for implementation of the Medicare Drug Price Negotiation Program (Medicare DPNP).

IVI is a 501(c)3, non-profit research organization committed to advancing the science, practice, and use of health technology assessment (HTA) in health care. Founded in 2017, the organization includes members from the research, patient, payer/purchaser, clinician and innovator stakeholder communities. IVI's work emphasizes collaboration and exploration of new solutions in pursuit of a U.S. learning healthcare system supported by patient-centered HTA and focused on high-quality, efficient, innovative, and equitable care for all people and communities. We believe this is only possible with a fundamental shift to resource allocation, coverage, and access-related decision-making that aims to maximize value for all stakeholders—particularly patients and other covered individuals.

Our work is guided by our Principles for Value Assessment.¹ These principles apply not only to the narrow context of HTA, but are the foundation of a patient-centered and equitable health system based on value to all stakeholders. The implementation by CMS of the Medicare DPNP should be grounded in these principles, the foremost among them being patient-centricity, transparency, equity, and vigorous methods enhancement.

IVI recognizes that the legislation includes specific guidelines and places limitations on implementation of the DPNP, and we commend CMS for its efforts to develop thoughtful and thorough guidance under considerable time constraints. Examining the initial guidance for the DPNP through the lens of IVI's core principles raises a number of concerns with both immediate and long-term implications, including:

¹ Full description of our Principles for Value Assessment in the U.S. available at:
<https://thevalueinitiative.org/principles-for-value-assessment-in-the-us/>

- The guidance fails to incorporate multiple elements needed to advance health equity, deliver value to patients, and influence the evolution of health research and healthcare delivery to support value-based decision making.
- The processes for comment, evidence collection, and assessment of included drugs raise a number of immediate concerns.

We appreciate the opportunity to offer comments and suggestions in the following areas:

Focus of DPNP should be on maximizing value, not simply minimizing prices

To the extent allowed by existing legislation, the DPNP should emphasize understanding and maximization of value—as opposed to simply minimizing product prices—as a primary objective of the program and orient program guidelines around this objective.

As the largest health insurer in the U.S., Medicare policy or programmatic changes have the potential to shape the structure of the U.S. health system at all levels. As such, CMS implementation of the relevant sections of the Inflation Reduction Act (IRA)—and particularly related to the DPNP—presents an opportunity to establish an inclusive and forward-thinking approach that emphasizes negotiations and decision-making based on maximizing value to Medicare enrollees, the Medicare system, and American society, rather than simply on minimizing unit prices.

The initial guidance for the Medicare DPNP, reflecting the emphasis in sections 11001 and 11002 of the IRA on price, outline a process constructed around the primary objective of negotiations to reduce prices for high-cost drugs and minimize costs to Medicare. Price does not equate to value. Rather, price (and costs as a result) is one of multiple components of value. This narrow focus on price as opposed to more comprehensive assessments of value risks perpetuation of decisions that shape patients' care based on budget concerns rather than value.

Value is multi-faceted, and CMS should endeavor to include a broader set of outcomes and other elements influencing value for Medicare and its enrollees when considering any benchmark price for negotiations. Data elements required by CMS per section 50.1 of the initial guidance are not sufficient to determine a price based on the value of the drug. Additional elements of value that reflect impacts on different stakeholders should be considered. For example, patient-level elements may include financial impacts of care, burden on family caregivers, and patient goals for treatment.² As a public

² See for example:

Wilson, M., Thavorn, K., Hawrysh, T. et al. Engaging Patients and Caregivers in an Early Health Economic Evaluation: Discerning Treatment Value Based on Lived Experience. *PharmacoEconomics*. 2022;40:1119–1130. <https://doi.org/10.1007/s40273-022-01180-4>

program, broader societal elements are also important to consider. Some examples include incentives for innovation, impacts on health equity, and insurance value.³

Implementation of the Medicare DPNP will establish a formal approach and framework that sets a precedent for both CMS and private sector approaches to price negotiations and decisions about coverage and access. We strongly encourage CMS to incorporate broader concepts of value into assessments and negotiations to the greatest extent possible, and to clearly articulate these considerations in the final guidance.

Health equity must clearly inform all aspects of DPNP guidelines

Equity implications of all aspects of the program should be systematically considered as part of DPNP activities, and strategies to support equity (by including members of underrepresented or “specific” populations as formal partners in the process, for example) should be incorporated wherever possible.

Health equity is the first pillar of the Centers for Medicare & Medicaid Services’ (CMS) Strategic Plan,⁴ which states:

CMS is working to advance health equity by designing, implementing, and operationalizing policies and programs that support health for all people served by our programs by incorporating the perspective of lived experiences and integrate safety net providers and community-based organizations into our programs.

Regarding the Center for Medicare (CM), it goes on to state:

As one of the largest payers in our health care system, CM is catalyzing delivery system transformation by issuing policies that advance equity across all Medicare programs and activities ... and consistently engaging people with Medicare throughout the policy process.

In the initial guidance neither the word “equity” nor related terms appear in the text. As a highly visible and novel program within Medicare, it is imperative that the DPNP reflect the objectives and practices outlined in the CMS strategic plan.

IVI recently completed Phase 1 of its Health Equity Initiative, a multi-stakeholder-driven process that aims to identify actionable changes to HTA processes, methods, and

dosReis, S., Butler, B., Caicedo, J. *et al.* Stakeholder-Engaged Derivation of Patient-Informed Value Elements. *The Patient*. 2020; 13:611–621. <https://doi.org/10.1007/s40271-020-00433-8>

³ Lakdawalla DN, Doshi JA, Garrison LP, Phelps CE, Basu A, Danzon PM. Defining Elements of Value in Health Care—A Health Economics Approach: An ISPOR Special Task Force Report [3]. *Value in Health*. 2018;21(2):131-139.

⁴ Source: CMS Strategic Plan Fact Sheet. Pillar: Health Equity. <https://www.cms.gov/files/document/health-equity-fact-sheet.pdf>

communication that acknowledge and resolve existing health disparities in research and healthcare decision-making.⁵ Many of the key themes arising through this ongoing process have implications for the Medicare DPNP, for example:

- **Fundamental change:** Incremental changes (“tinkering around the edges”) are insufficient to address the systemic issues impacting equity
- **Accountability:** Change will not occur without accountability for and to all stakeholders
- **Meaningful engagement:** All actors—and especially underrepresented communities—must be meaningfully engaged throughout the process, including decision-making.
- **Data and methods:** Incomplete evidence and imperfect methods are not an excuse to continue practices that perpetuate bias or inequities. A “learning laboratory” approach is needed for testing methods (especially mixed quantitative/qualitative) and identifying evidence gaps.
- **Transparency:** Transparency is a necessary condition for both trust and accountability—particularly as an antidote to lack of trust of marginalized communities for researchers, providers, and decision-makers—and critical to the advancement of health equity.

Many of these findings, which largely align with the priorities and planned actions outlined in the CMS strategic plan, have direct application to the Medicare DPNP. In all aspects of planning and execution of the Medicare DPNP, health equity should remain a principal concern and the lens through which decisions are made, with consideration at minimum of:

- **Implications of external factors for equity**—underrepresentation of specific groups in data, for example.
- **Alignment of practices and guidelines with equity goals**—ensuring DPNP process reflects actions outlined in CMS strategic plan and recommendations from IVI’s work. For example, engaging members of underrepresented communities as collaborators.
- **Downstream equity implications of DPNP processes**—deliberate consideration of potential equity impacts now and in the future, including implications for access and affordability, and potential influences on the private market.

⁵ More information available at: <https://thevalueinitiative.org/health-equity-initiative/>

IVI strongly recommends revision of the DPNP guidance to align with CMS's strategy, positioning health equity at the forefront by clearly outlining specific actions including:

- **Process for evaluating potential bias and equity implications of evidence.**
- **Creation of enrollee advisory groups**, including patients and other members of diverse communities with relevant lived experience, with explicit opportunities to participate in specified stages of negotiations.
- **Calling for and incentivizing evidence generation and data collection** with underrepresented populations.

Systematic approaches to elevating patient voices are needed

Affected beneficiaries (e.g., current patients), their families and caregivers, and organizations that represent them must be actively involved in DPNP processes with a meaningful voice in decision making, and specific measures to ensure patient experience and other inputs are elevated in CMS's evaluation of candidate drugs must be explicitly outlined in the guidance.

IVI appreciates the steps taken in the initial guidance to provide opportunities for patients, their families and caregivers, and organizations that represent them to provide input or submit evidence to support DPNP negotiations. We are concerned that the initial guidance fails to include mechanisms for patient engagement beyond evidence submissions and does not include guidelines or processes to ensure evidence from patient experience, qualitative or quantitative, is incorporated alongside other evidence such as clinical trial data.

Formal mechanisms for patient engagement in negotiations should be included to provide essential guidance and context from lived experience, such as a treatment-specific advisory group formed for each drug following its selection for negotiation. Mechanisms for inclusion of patient stakeholder voices are also a key tool for advancing health equity. Inclusion of members from diverse populations and backgrounds to serve on patient advisory groups provides members of historically underrepresented communities an important opportunity to have a voice in the process.

Engaging patients in dialogue or soliciting input from patients and other affected populations is necessary but not sufficient, however. It is critical that CMS explicitly include measures throughout the DPNP processes to ensure patients have equal standing as stakeholders and participants in decision making. In the case of a patient advisory body, guidelines should outline the topics within the group's scope, including how input and recommendations will be documented. Most importantly, the guidelines should identify specific points in DPNP processes where advisory groups have complete or partial decision authority and provide a detailed outline of these processes.

Similar steps are required to ensure that evidence submitted on patient experience, patient preferences, and similar topics is included in negotiations, especially in the context of determining unmet need, degree of therapeutic advance, and comparison to alternative therapies. Such evidence is frequently dismissed or discounted in similar contexts due to perceived lack of rigor relative to other evidence or lack of experience incorporating qualitative data. DPNP guidelines should specify measures to ensure consistent inclusion of patient experience data.

Measures include:

- Inclusion of patient researchers in CMS evaluation teams.
- Explicit frameworks for evaluation of evidence and weighting in reviews.
- Guidelines for mixed-method approaches designed to account for qualitative evidence.

Clarity and specificity in methods and overall approach are needed

While a “qualitative approach” to evaluating evidence on a given drug provides CMS staff with needed flexibility, greater transparency into this process is needed.

As a research organization grappling daily with the challenges and complexity of comparing medical technologies in the context of HTA, IVI recognizes the need for flexibility in CMS’s approach (as outlined in sections 50 and 60) when evaluating evidence, conducting analyses, and evaluating therapies in negotiations. To ensure transparency, predictability, and consistency, however, a flexible and “qualitative approach” should be conducted within a methodological framework describing types of data and evidence to be used, guidelines for evaluating and prioritizing evidence, procedures for engagement with external parties, methodological guidelines (especially for mixed-method approaches), and other relevant subjects. Articulating these considerations will provide consistent guidance to CMS teams working in varied therapeutic areas, increase the relevance and usability of evidence submitted to CMS, and provide the transparency necessary to ensure both rigor and accountability.

As part of this descriptive framework, the initial guidance should include greater detail on a number of methodological subjects, including:

- **Therapeutic advance:** Provide clear definition and outline the methods for measurement and evaluation
- **Clinical benefit:** Provide more details on how “clinical benefit” will be translated into “adjusting the starting point” for negotiations. For example, adjustment amount and how patient input will contribute to this definition
- **Unmet need:** Provide clear definition, including steps for consideration of health equity, and outline the methods for measurement and evaluation

- **“Other factors” to be considered:** Further define what “other factors” CMS would consider. These should include patient lived experience as well as additional elements of value, including both patient-level elements, for example non-clinical and economic impacts, caregiver burden, and patient preferences. and elements of value from the societal perspective, including scientific spillovers, impacts on innovation, real-option value, insurance value⁶
- **Modeling and analysis:** Describe whether and in what ways simulation modeling, decision analyses, or other approaches may be used for therapy evaluation

Finally, the potential discriminatory effects of the quality-adjusted life year (QALY) are well-documented, but it remains the most widely accepted methodological tool for incorporating impacts on quality of life alongside life extension. The guidance currently underscores the risks of discrimination without recognizing this methodological need, describing ongoing efforts to identify other potentially discriminatory metrics for exclusion from CMS consideration. The guidance fails to recognize both the methodological role of the QALY and the importance of developing alternative methodologies. CMS should revise the guidance to reflect these considerations, encourage research to advance alternative metrics, and outline a process for considering use of new metrics in DPNP negotiations. The guidance also states that CMS will consider evidence from studies where the QALY evidence is “clearly separated,” but the meaning and intent of this statement are unclear. Greater clarity is needed to prevent confusion on the part of researchers and stakeholders interested in submitting evidence, and to ensure evidence submitted is aligned with CMS expectations.

DPNP guidance must be informed by forward-looking strategic considerations

In an environment where availability of evidence and methodologies lags behind the needs of comprehensive value assessments, CMS must endeavor to spur innovations that advance the field, for example, by calling for data on relative treatment effects across patient subpopulations and encouraging exploration of novel methods to capture quality-of-life outcomes as an alternative to QALYs.

IVI is founded on the belief that a patient-centric, value-driven healthcare system is possible with the collaboration, inclusion, and investment of all stakeholders. CMS has a unique opportunity to move that vision forward in its implementation of the Medicare DPNP.

We call on CMS to embrace this opportunity. The steps implemented to engage and include diverse populations of patients in negotiation processes can set a higher standard for private health plans. Demonstrating mixed-method approaches to

⁶ See footnotes 2 and 3 for relevant references.

April 14, 2023

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evaluation may drive increased incorporation of patients' lived experience, while the outcomes and other factors considered in the process will shape both the priorities of the research community and the evidence it produces.

We appreciate the opportunity to provide input on this important issue. Please do not hesitate to contact me or Mark Linthicum, Director of Policy, at mark.linthicum@thevalueinitiative.org for further discussion.

Sincerely,

A handwritten signature in dark ink, appearing to read 'Jason', with a long horizontal flourish extending to the right.

Jason Spangler, MD, MPH, FACPM
Chief Executive Officer
Innovation and Value Initiative

To: Centers for Medicare and Medicaid Services
Re: Medicare Drug Price Negotiation Program Guidance

The Institute for Clinical and Economic Review (ICER) is pleased to provide comments on the [Medicare Drug Price Negotiation Program Guidance Initial Memorandum](#). ICER is an independent non-profit research organization that evaluates medical evidence and convenes public deliberative bodies to help stakeholders improve patient outcomes and control costs. Our reports are used by the Veterans Administration and by most Medicaid and private insurance plans to help inform their formulary determinations and to support drug price negotiation. As part of the international community of health technology assessment organizations, we also participate in many activities related to the development of methods of evidence assessment, cost-effectiveness analysis, and public deliberation that can support governments in achieving affordable access to high-value care.

We have comments related to several key issues within the draft guidance:

Issue 1: Section 50.2. “CMS is soliciting comment on other metrics, in addition to QALYs, that may treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill and that CMS should also exclude from consideration when developing offers and reviewing counteroffers.”

Comment: There are widely-recognized metrics other than the QALY that can be used for comparative clinical effectiveness and cost analyses that meet the intent of the IRA statute. Prominent among these alternatives is the “equal value of life years gained,” or evLYG. The evLYG was designed to weigh the value of extended life of all individuals in exactly the same way, with each year of life gained from treatment valued the same, thereby eliminating any risk of valuing extended life lower for conditions in which people are elderly, disabled, or terminally ill. The evLYG metric is not the only non-QALY alternative that meets this standard, but the evLYG has served for many years as the bedrock of ICER’s drug price benchmarks that are used by the Veterans Administration, Medicaid programs, and most private insurers. The evLYG has also gained acceptance in state legislation as a non-discriminatory alternative to the QALY, and legislative language allowing the evLYG has been supported by a prominent disability rights group in Massachusetts. We provide further rationale that support the view that the evLYG is consistent with IRA statute and will be helpful for CMS in its deliberations below.

Recommendation: *We propose that CMS clarify that research using non-QALY alternatives such as the evLYG that value each year of extended life equally, irrespective of whether an individual is elderly, disabled, or terminally ill, meet the statutory standard for consideration by CMS in its drug price negotiations under the IRA. CMS should stipulate, however, that it will not consider any evidence that separates populations eligible for treatment into subpopulations by age or level of ability/disability to generate different findings for the purposes of determining the maximum fair price.*

Further Rationale:

- 1. *The evLYG measure was developed specifically to address concerns about the QALY. It values any extended life from treatment in the same way for all individuals.***

CMS is likely to hear from some groups that there is no summary measure of health gain that meets the statutory standard, or that there are potential measures that would be non-discriminatory but that are in development and have not been previously used or accepted by the broader health economics community. We argue that there are measures that meet the statutory language and intent that are ready for use as part of the evidence that can help CMS construct and justify initial price offers. Specifically, the [equal-value of life years](#) gained (evLYG) metric was designed with the explicit intent to address concerns about the QALY's potential to devalue extended life. The first-known version of the evLYG was created by [Nord et al.](#), who more than 20 years ago developed the "equal value of life" measure in which any extension of life attributed to an intervention is valued at a quality-of-life weight of 1, or ideal health. This measure did not gain widespread use, and since Nord's efforts, most approaches to addressing discrimination concerns regarding the QALY have emphasized the role that deliberative processes should play in integrating important social values into any application of cost-effectiveness to public policy. However, in 2018, recognizing the concerns about the QALY from some patient groups and policymakers, we developed a variation of Nord's earlier approach that we named the evLYG. The key difference between the evLYG and QALY is that the evLYG assigns a single, uniform utility (i.e. rating of quality of life) to each increment of extended life provided by an intervention compared to its comparator. Unlike Nord, the evLYG does not assign a utility of unrealistic ideal health to time during life extension. Instead, the evLYG assigns to time in extended life a utility that reflects the norm of the entire U.S. general population. No matter the age or health status of patients with the condition, if a treatment extends life it will be credited with the same value for each unit of time. Some commentators have claimed that the evLYG meets concerns about discrimination by the QALY by sacrificing the ability to measure quality of life, but this is a misunderstanding. The evLYG treats extended life in the same way across all conditions but also fully values the relative effects of different treatment options on improvements or decrements in quality of life during all time that is not attributed to an intervention's added survival.

- 2. *Leading academics affirm that the evLYG values extended life in a non-discriminatory fashion consistent with IRA statute.***

Richard Frank and Len Nichols, leading health economists associated with Brookings Institution, recently shared their thoughts on [threats to Medicare's new drug negotiation power](#) and highlighted that the evLYG has been "employed in numerous settings for reasons precisely consistent with Congressional intent and would be available to HHS for use in the negotiations set out in the IRA." Other academics have voiced similar views. Peer-reviewed [research](#) conducted by University of Washington academics confirms that the evLYG and another non-QALY measure of health gains named the Health Years in Total weigh any time of extended life the same for all individuals. This

means that there is no risk of devaluing a treatment for anyone, including the elderly, disabled, or the terminally ill. Further, leading cost-effectiveness academics at Tufts University have recently published an [article](#) emphasizing that the evLYG and Healthy Years in Total “place the same value on additional years of life across diseases and populations.” In an [earlier article](#), these academics specified that “For those uncomfortable with QALYs, evLYG assessments offer what they might regard as “fair” or “equal” evaluations, assigning an equal value to life extension regardless of the patient’s current state of health.

There are potential limitations to any summary measure of clinical effectiveness that combines the impact of treatment on length of life and quality of life, but the evLYG has been acknowledged by academics as an alternative to the QALY that meets the primary goal of valuing extended life the same way for all individuals, thus avoiding the QALY’s risk of discrimination in valuation of extended life for treatments of the elderly, people with disabilities, and the terminally ill.

3. *Leading disability groups have not labeled the evLYG as being discriminatory, and in at least one case have supported legislation with language that would clearly allow use of measures that value extended life in a manner consistent with the evLYG.*

The [National Council on Disability](#) (NCD) produced a report on the QALY and its “devaluation” of life with disability. In that document they mention the evLYG but do not label it as discriminatory. In a subsequent [report](#), the NCD evaluated non-QALY alternatives, and while they comment on potential limitations of the evLYG and all other non-QALY alternative measures, they do not label the evLYG as discriminatory. On page 8 of this report, they acknowledge that the evLYG values extended life the same for all individuals: “Under ICER’s modified version of the EVL approach, the evLYG, any extension of life is valued the same across every population, at a quality-of-life weight of the general population.” Similarly, the Disability Rights Education & Defense Fund published an earlier [report](#) in 2021 that does not describe the evLYG as discriminatory. In fact, the authors of this report note on page 6 that “the evLYG eliminates the risk of undervaluing life-extension for people with disabilities...”

Finally, in Massachusetts, the Disability Policy Consortium, a major organization advocating for the disability community, is a leading supporter of a Crisis Standards bill ([H.1180](#)) containing language that would prohibit the use of the QALY while firmly allowing use of the evLYG and other similar measures that do not devalue extended life from treatment. This language is shown below:

For any public or private entity, or agency of the commonwealth, when determining whether a healthcare treatment should be available within a formulary, or determining the value of a healthcare treatment, to employ a measure or metric which assigns a reduced value to the life extension provided by a treatment based on a pre-existing disability or chronic health condition of the individuals whom the treatment would benefit.

This language was developed in discussions between the Disability Policy Consortium and ICER in 2022 with an explicit mutual acknowledgment that it would prohibit the QALY while allowing use of the evLYG as an alternative that would not have discriminatory implications for people with disabilities. Thus, the evLYG stands out as a metric that was developed to address the risk of devaluation of extended life and has been viewed by multiple groups advocating for people with disabilities as not having the same discriminatory risk posed by the QALY.

- 4. Several states have adopted legislation to guide prescription drug affordability reviews with safeguard language that has the same intent as that in the IRA: prohibiting the QALY but retaining the ability to use other measures such as the evLYG that do not devalue extended life for the elderly, those with disabilities, or those with terminal illness.**

Several states have considered ways to address prescription drug costs using measures other than the QALY. Following testimony from disability groups and others, Washington state passed a law creating a [Prescription Drug Affordability Board](#) with safeguard language prohibiting the QALY that would still allow measures such as the evLYG: “The methodology determined by the board must not use quality-adjusted life years that take into account a patient’s age or severity of illness or disability to identify subpopulations for which a prescription drug would be less cost-effective. For any prescription drug that extends life, the board’s analysis of cost-effectiveness may not employ a measure or metric which assigns a reduced value to the life extension provided by a treatment based on a preexisting disability or chronic health condition of the individuals whom the treatment would benefit.” Oregon has also established a Prescription Drug Affordability Law with [similar language](#) that would prohibit use of evidence based on the QALY but allow research based on the evLYG: “For any prescription drug that extends life, the board’s analysis of cost-effectiveness must weigh the value of the quality of life equally for all patients, regardless of the patients’ age or severity of illness or disability.”

These laws and some pending legislation, such as that establishing a Prescription Drug Affordability Board in [Vermont](#), are good examples of how state authorities designing safeguards with the same intent of the IRA statute have adopted similar yet more detailed terms that would prohibit use of the QALY while retaining the ability to use summary measures such as the evLYG to support comparative clinical effectiveness and cost comparisons that are essential to the full function of a drug price negotiation effort.

- 5. CMS has already stated that it intends to consider measures of treatment success such as “survival.” The evLYG incorporates considerations of the number of years gained from treatment in the same way as this widely-accepted measure.**

In section [60.3.3.1 of the CMS Initial Guidance document](#), CMS provides information about measures that will be included within the scope of comparative effectiveness evidence: “CMS intends to consider health outcomes, intermediate outcomes, surrogate endpoints, patient-reported outcomes, and patient experience when reviewing the clinical benefit of the selected drug and its therapeutic alternative(s). When reviewing such information, as noted above CMS will not

use evidence in a manner that treats extending the life of any individual as lower value than the life of another individual; this includes QALYs when used in association with life extension. Health outcomes such as cure, **survival**, progression-free survival, or improved morbidity could be considered when comparing the selected drug to therapeutic alternatives.”

Common comparative survival outcome measures, such as 5-year survival among patients with cancer, are expressed as life years gained when comparing the selected drug and its therapeutic alternative(s). 5-year survival therefore varies and is influenced by the starting age among individuals who take the same drug. But it seems unreasonable to argue that survival measures could therefore be used “in a manner that treats extending the life of any individual as lower value than the life of another individual.” 5-year survival outcomes weigh extended life in the same way – each year of extended life is counted as a year no matter what the condition is or how old the patients are with that condition. This is the same approach used by the evLYG. By specifying in the draft guidance that survival and thus life years gained would be considered as part of the evidence on comparative clinical effectiveness, CMS is demonstrating its reasonable interpretation that extended life can be measured fairly across conditions and individuals of different ages. This interpretation would encompass the conclusion that the evLYG does not treat extended life as lower value for the elderly any differently than 5-year survival outcome measures.

Issue 2: Section 60.3.2. “Specifically, CMS is soliciting comments on the advantages and disadvantages of using net prices and/or ASPs as the starting point for the initial offer for selected drugs with at least one therapeutic alternative and the Federal Supply Schedule or Big Four price for selected drugs with no therapeutic alternative or for selected drugs with therapeutic alternatives with net prices and/or ASPs greater than the statutory ceiling. CMS is also soliciting comment on other starting points for the initial offer, including but not limited to other domestic reference prices, along with their disadvantages and advantages. Lastly, in the event that there are multiple therapeutic alternatives for the selected drug, CMS is soliciting comment on how to consider the range of net prices and/or ASPs and utilization of each therapeutic alternative to determine a single starting point for developing the initial offer.” (p. 49-50).

Comment: CMS faces a difficult challenge in designing a consistent process for determining relevant comparators and using comparisons with those comparators to arrive at the initial offer that reflects the overall goal of achieving “the lowest maximum fair price for each selected drug.” Reference pricing has been proposed by CMS as the anchor to its approach. Reference pricing can be done “internally” within the prices paid by a single payer for a set of drugs, with the general intent being to reduce the price of a particular drug to that of a lower priced, equivalently effective drug. Reference pricing can also be used to describe an “external” approach of selecting a lower price for a given drug from among the prices paid by other payers, as in international reference pricing. For the purposes of our comments and recommendations below, we will primarily focus on internal reference pricing within a set of drugs paid for by CMS, but we recognize that CMS is also considering external reference pricing to prices paid by other payers such as the VA and the Big Four, and may receive comment suggesting even broader external reference pricing to foreign countries.

Internal reference pricing of a drug against its comparators is relatively straightforward when the evidence is judged not to demonstrate any clinical advantages for the drug in question. In that case, the drug can be set at the same price as the comparator or a “basket” of comparator drugs. But real problems arise when there are no drugs that can be viewed as reasonable clinical comparators. It is also problematic to use internal reference pricing to a single or multiple comparators when these comparators themselves are priced far above reasonable value in relation to their clinical benefits for patients.

One could argue that the conceptual intent of the IRA drug negotiation statute was to address the market “failure” that occurs when a drug has no generic or biosimilar competition despite many years in the market. Following that logic, it would seem reasonable to assume that simple reference pricing to other brand name drugs, or even reference pricing outside CMS to lower prices paid for the same drug by the VA or the Big Four, would not represent what a true “generic” price should be. Therefore, some might argue that CMS should decide that lowest maximum fair price for every drug will be a price reflecting only the marginal cost of production of the drug today, with some slender “profit” margin on top. However, this approach would be the most radical available to CMS, and the downside to this “generic pricing” model is that it would reduce prices so dramatically that the manufacturer might see

little reason to continue marketing the drug. For that reason, other alternatives should be considered, although one could still argue that if a drug under negotiation has multiple comparators with the same mechanism of action and identical side effect profiles, a true generic pricing approach would not present a great risk to patients given that they could switch to other drugs with comparable outcomes if the manufacturer chooses to remove the drug under negotiation from the market.

If a true generic pricing approach is not taken, how else could CMS apply a consistent approach to determine a maximum fair price lower than the ceiling price established by statute for a drug that is superior to its comparators? CMS could develop an arbitrary system in which it assigns a certain % higher price over the comparator for each categorical degree of clinical superiority. For example, a drug determined to be “incrementally” superior could get 10% higher price than its comparator, whereas a drug that is “moderately” superior could get 15% higher pricing. But there is no economic justification for any particular magnitude of % increases unless the increases are scaled to the magnitude of the clinical benefit in a reliable, transparent manner. In addition, a blunt % additive approach would also fail to address the problem of pegging prices for negotiated drugs to comparators that are themselves overpriced in relation to clinical value.

This is where cost-effectiveness techniques offer advantages that could prove useful. Value-based, or “threshold” prices could be generated for every drug under negotiation, whether there are no comparators or multiple comparators. These results could supplement any reference pricing approach to provide an alternative set of prices to consider as an initial offer price. When the judgment of the clinical evidence is that there are no meaningful differences between a drug under negotiation and its comparator, the results of internal reference pricing and cost-effectiveness threshold pricing will be essentially the same; but when there are advantages and/or disadvantages between the drugs, a cost-effectiveness threshold price can give a scaled pricing recommendation that would provide CMS with additional evidence-based options from which to select an initial offer price. In the Recommendations below we set out a brief description of how cost-effectiveness analysis could be woven into the CMS process and address several of the conceptual and practical challenges that would be involved.

Recommendations:

No matter what method CMS ultimately uses, there will be three main phases: 1) determining the indication(s) and comparator(s); 2) judging the evidence; and 3) using the evidence to determine prices eligible for consideration as the initial offer price.

1. Determining the indication(s) and comparator(s).

Determining comparators for clinical and cost comparisons will be one of the most challenging aspects of determining an initial offer price. There are three different situations: 1) no active drug comparator; 2) a single drug comparator; and 3) multiple comparators. In some situations, it may be that some patients with a condition are treated with surgery or a procedure whereas others are treated with a comparator drug. This is the case, for example, with hypertrophic cardiomyopathy. Whether patients may be treated with other drugs, surgery/procedures, or just “supportive care,” CMS will face difficult

choices about which alternative treatment options should serve as formal comparators. If too many comparators are selected, the burden on both the drug maker and CMS gathering and evaluating evidence could become extreme. And the number of comparators for each drug under negotiation may expand with the number of indications that CMS decides to evaluate as part of its determination of an initial offer price. We therefore propose the following decision rule as one that CMS could adopt to create a consistent and transparent approach that still leaves enough flexibility to manage less common situations. Thresholds for selection of indications and comparators are arbitrary but are suggested as representing a compromise between the goals of comprehensiveness and feasibility:

- A. For drugs with multiple indications, if the most common indication accounts for >75% of use among Medicare beneficiaries then CMS can perform its entire evaluation based on that single indication. If this is not the case, then CMS should select the top two indications by use among the Medicare population. This information should be determined by analysis of CMS data.
- B. For each indication, CMS should select no more than two comparators for determination of its initial offer price.
- C. The first comparator should be the lowest cost alternative treatment recognized as a reasonable alternative by clinical guidelines and/or the expert opinion of specialist clinicians and patient groups, whether that treatment is another drug, a procedure/surgery, or supportive care. CMS may wish to set a minimum use threshold for eligibility of a potential comparator to ensure that comparators have face validity with clinicians and patients.
- D. The second comparator should be the second lowest cost alternative treatment recognized as a reasonable alternative for use in that indication by clinical guidelines and/or the expert opinion of specialist clinicians and patient groups.
- E. Instead of the second lowest-cost alternative treatment, CMS could consider selecting as a second comparator the most commonly-used alternative treatment. The advantage of this approach is that it would enhance face validity with clinicians and patients and may be more likely to be more similar in its level of benefits and risks to the drug under negotiation, facilitating a simplified reference pricing approach. The disadvantage of this approach would be the risk that the most commonly-used alternative is not reasonably priced itself, limiting the ability of CMS to identify a lower price that would be reasonable to consider as a maximum fair price.

2. Judging the evidence.

Once the indication(s) and comparator(s) have been determined, the next phase requires CMS to judge the evidence on comparative clinical effectiveness. For this purpose, CMS can choose to emphasize comparisons of individual clinical outcomes, including both benefits and harms. However, CMS may also find it useful, especially when drugs under negotiation and their comparators have differing sets of benefits and/or harms, to evaluate comparisons of summary clinical outcomes such as the evLYG. Summary measures will provide another perspective on what will otherwise be a relatively qualitative comparison of the overall net health benefit provided by the drug under negotiation and its comparators.

CMS also has the choice on whether to use qualitative language to describe its judgment of the evidence or to use discreet categories of comparative clinical effectiveness. For example, health technology agencies in Germany and France, and ICER in the US, have categories of comparative clinical effectiveness, such as “comparable” or “minimal added benefit.” Making a categorical determination of this type requires a clear set of categories with general language distinguishing the thresholds between them. CMS may not have time to develop a new scheme of this type and so may wish to consider adopting one of the existing frameworks. One advantage of an ordered categorical approach is that it creates a mechanism for greater reliability and transparency of decision-making versus qualitative language alone. Another advantage is that categories of comparative clinical effectiveness can be linked explicitly to reference pricing, with each category associated with a specific price % difference (if any) from the comparator. The downside of a categorical approach is that it is difficult to combine considerations of benefit, risk, and uncertainty in a way that provides adequate flexibility for different comparisons, but our judgment is that CMS will be able to support its rationales for initial offer pricing more effectively if it adopts a categorical approach to judging the evidence on comparative clinical effectiveness versus qualitative language alone.

3. Using the evidence to determine the initial offer price.

Once the evidence on comparative clinical effectiveness has been judged, CMS can translate that into initial offer prices through several mechanisms, each of which, under different circumstances, may offer the preferred route to a lowest maximum fair price. We propose that CMS would benefit from adopting two mechanisms: 1) a reference pricing approach; and 2) a cost-effectiveness threshold approach.

Each of these mechanisms would function differently depending on the nature of the comparator(s) and the judgment of the comparative clinical effectiveness. A reference pricing approach is easiest when CMS judges the evidence not to demonstrate clinical superiority of the negotiated drug over its comparator. In that case, reference pricing would suggest that the price of the negotiated drug should be set at the same level as the comparator. A cost-effectiveness threshold approach, however, would allow both the negotiated drug and its comparator to be compared to each other and to care without active treatment. This kind of analysis may suggest that both drugs are overpriced in relation to their added clinical benefits, and therefore suggest an initial offer price even lower than the reference price of the lowest cost comparator. Having both a reference price and a cost-effectiveness threshold price would provide CMS with perspective on fair pricing and on their choices for framing an initial offer price.

The advantages of having both mechanisms provide potential initial offer prices are even clearer when the negotiated drug is judged to be clinically superior to its comparator. As noted earlier, even a categorical reference pricing method cannot provide a consistent, transparent mechanism for suggesting an initial offer price unless an arbitrary “added % price” is determined for each category of comparative clinical effectiveness. Cost-effectiveness threshold pricing, however, consistently translates added clinical benefit into a price that is scaled in a consistent, transparent manner over the price of the comparator. CMS could consider a single cost-effectiveness threshold price or a price range by using

traditional cost-effectiveness ranges of \$100,000-\$150,000 per evLYG. As noted earlier, having potential initial offer prices generated through a reference pricing approach and a cost-effectiveness threshold approach gives CMS more flexibility to address all the different permutations of comparators and judgments about comparative clinical effectiveness. Using both methods would give CMS the tools to address situations when there are no true comparator drugs and when the prices paid for comparators or the prices paid by the VA or other Big Four entities do not adequately represent prices commensurate with the clinical value of the negotiated drug.

The primary challenge with adopting a two-method approach is that CMS is not staffed to develop cost-effectiveness models for all the drugs it will be negotiating, at least for this first cycle. If a cost-effectiveness threshold approach is considered, the first cycle of negotiation would need to rely on cost-effectiveness results from outside sources or from the drug makers themselves. Even if CMS is not fully prepared to generate or vet cost-effectiveness information in this first cycle of negotiation, we would propose that it set out guidance that would allow for this function in the future, and that in the short term it seeks to build enough internal capacity to vet the cost-effectiveness results that may be submitted by drug makers themselves.

In summary, we encourage CMS to develop as clear a process as possible, with decision algorithms that provide external clarity for drug makers and other stakeholders while buttressing CMS's ability to justify the rationale for its initial price offers on each negotiated drug. We believe that categorical approaches to judging comparative clinical effectiveness will best support a broader effort to enhance consistency and transparency, and we propose that a dual mechanism of reference pricing and cost-effectiveness threshold pricing be implemented to give CMS the full range of evidence-based tools to translate comparative clinical effectiveness judgments into initial price offers under differing scenarios of drugs, indications, and comparators.

Issue 3: In the Section 60.3.2, CMS suggests benchmarking prices based on net prices for Part D drugs with at least one therapeutic alternative.

Recommendation: We suggest that any starting position, such as the net prices for Part D drugs, be freely available to the public. Without open public access to Part D drug net pricing, it will be challenging for CMS to receive actionable public comment on comparative analyses given the starting point will be unknown.

Issue 4: In Section 60.3, CMS is silent on whether or not a drug that is associated with health system cost offsets (e.g. reduced hospitalization costs or reduced health care services) when compared to its therapeutic alternative shall be a factor in drug price negotiation. Economic theory and corresponding value assessment best practices support the inclusion of health system cost offsets in estimating a value-based price.

Recommendation: We suggest CMS request evidence beyond the net price of therapeutic alternatives to include all health system costs associated with the drug of interest and its therapeutic alternatives.

Issue 5: In Section 60.3.3.2, CMS provides the following interpretation of unmet medical need, “A selected drug will be considered to meet an unmet medical need for an indication included in the analysis in cases where limited or no treatment options exist.”

Recommendation: We suggest CMS allow for a broader definition of unmet medical need to include situations when treatment options may exist, but the patient population remains far from achieving the health of the general US population. Methods exist whereby unmet medical need is quantified through [shortfall](#) approaches that compare the general population’s expected health to that of the patient population prior to the introducing the health impacts from the drug of interest. These shortfall calculations can be done with non-QALY measures of health gain such as the evLYG or Healthy Years in Total.

Sincerely,

Jon Campbell, PhD, MS
Senior Vice President for Health Economics
Institute for Clinical and Economic Review

Steven D. Pearson, MD, MSc
President
Institute for Clinical and Economic Review

April 13, 2023

BEFORE THE
CENTER FOR MEDICARE
CENTERS FOR MEDICARE AND MEDICAID SERVICES
DEPARTMENT OF HEALTH AND HUMAN SERVICES
Washington D.C.

RE: Medicare Drug Price Negotiation Program Guidance

Dr. Meena Seshamani
Deputy Administrator and
Director of the Center for Medicare
Department of Health and Human Services
7500 Security Blvd.
Baltimore, MD. 21244-1850

Dear Director Seshamani:

I and my colleagues at the Institute for Policy Innovation (IPI) would like to thank the Center for Medicare for this opportunity to comment on how pharmacy benefit managers affect drug access and affordability.

The Institute for Policy Innovation is a non-profit, non-partisan public policy “think tank” based in Irving, Texas, and founded in 1987 to research, develop and promote innovative and non-partisan solutions to today’s public policy problems. IPI is a public foundation, supported wholly by contributions from individuals, businesses and other non-profit foundations.

The Inflation Reduction Act, signed into law last year, introduced unprecedented changes to the Medicare Part D prescription drug benefit. For the first time, the government is empowered to directly negotiate prices for certain high-cost drugs covered by Medicare. On March 15, the Centers for Medicare & Medicaid Services released "initial" guidance describing how it proposes to implement its new price-setting authority.

What CMS proposes in this 91-page memo should alarm patients and physicians, as well as advocates for government transparency and accountability.

By way of background, I am a resident scholar with the Institute for Policy Innovation, a non-profit, non-partisan public policy "think tank" based in Irving, Texas, and founded in 1987 to research, develop, and promote innovative and non-partisan solutions to today's public policy problems. I am also a past president of the Health Economics Roundtable for the National Association for Business Economics, the largest trade association of business economists. The guidance sets forth vague standards for how it will identify which drugs are subject to price controls, while severely curtailing input from patients or their doctors. It grants vast discretion to government bureaucrats to decide the price-setting process, while requiring negotiations take place behind closed doors, leaving the public in the dark. Yet despite the momentous changes CMS envisions to Medicare -- changes CMS itself calls "novel" and "complex" -- it has limited the public comment period to just 30 days, half the time typically provided.

The Biden Administration justifies this power grab by claiming its drug pricing provisions will save the government \$237 billion over 10 years. Yet [according](#) to the nonpartisan Congressional Budget Office (CBO), government price controls largely achieve their lower costs by narrowing or restricting the choice of medications available to patients. Many analysts predict that the program will only achieve its savings targets if it forces patients to switch away from medicines they have relied on for months or years.

Medicare beneficiaries won't be the only ones impacted. Given the size of its patient population, Medicare will exert a significant downstream effect on private plans with its drug pricing decisions. All patients will feel the brunt of stifled innovation, as fewer new cures and treatments are developed.

A CBO [analysis](#) of a similar bill predicted that return on investment for new drugs would drop by 15 to 25 percent after Medicare price controls are implemented -- resulting in 30 fewer new medicines by 2029. An [analysis](#) by Tomas Philipson at University of Chicago predicted that 135 fewer drugs would launch by 2039.

The stakes are too high to prematurely cut off debate. Patients, physicians, and other stakeholders must have sufficient time to weigh in. Instead, CMS is trying to rush the process, ruling that certain key provisions in its guidance -- such as which types of drugs are eligible for price-setting -- are already "final" and thus not subject to *any* public feedback.

In some cases, CMS is even overreaching its statutory authority. Congress exempted from price negotiations drugs which have been on the market for fewer than nine years (for small-molecule drugs) or 13 years (for biologics) -- yet CMS claims it can negotiate prices for drugs that have not yet reached the end of the patent-protection period provided by Congress -- and again, argues that its determination is "final."

What space CMS does provide for patient and physician input is plainly inadequate. Under its proposed guidance, once CMS selects a drug for price negotiations, patients and physicians will only be invited to share their perspectives during a general "information collection request" (ICR). This ICR will take place before crucial data is shared, such as what treatment alternatives

are available or which drug indications or disease outcomes might be relevant. Using the ICR itself suggests the pro forma character of this process, as ICRs are typically used by the government to collect technical data. Clearly, CMS does not intend to place much value on patient or physician viewpoints.

How will CMS ascertain a drug's "fair" price? It proposes to compare a selected drug not to a bioequivalent, but to all drugs that treat the same condition or have a similar therapeutic effect. It will then base its price on the lowest-priced drug in that therapeutic class. This pricing scheme is supposed to shift drugmakers away from developing the so-called "me-too drugs" that follow on a medical innovation. Yet, as patients and doctors know all too well, medications are not interchangeable, and patients with the same disease may respond very differently to a particular drug. Besides, these so-called me-too drugs provide valuable competition for the original products. Many patients work with their physicians over a long period of time to find the right combination of medications that adequately treats their condition and limits side effects. Nor is a first-in-class drug necessarily the best. Lipitor and Crestor were the fourth and fifth statins approved by the FDA, yet these "me-too drugs" have proven more effective in treating heart disease than earlier medications.

But the public will not be privy to many key details on how the CMS determines a drug's price. CMS rules require that drugmakers keep confidential all negotiation discussions, including the price CMS offers and any justification it provides for its price. Moreover, drugmakers must destroy all information received from CMS during negotiations within 30 days after a drug no longer qualifies as a selected drug. These requirements would run afoul of FOIA and government record-keeping rules, and they could even constitute a prior governmental restraint on speech.

This lack of transparency will hinder efforts to hold government accountable. While drugmakers have a strict 30-day window to submit data on a drug and to accept an offer, CMS only has to share a public explanation for its price more than a year after soliciting initial feedback and six months after a drug's price is published. In the meantime, drugmakers will be muzzled by confidentiality rules from raising concerns about CMS errors or methodological problems.

The Inflation Reduction Act failed to reduce inflation, but it could jeopardize the rare government program that achieves high levels of public approval. A survey last year found that nearly 90 percent of seniors say they are satisfied with their Medicare Part D coverage. Yet the Biden Administration has proposed to radically change the program, potentially limiting patients' access to life-saving medicines and endangering future cures. Nearly 50 million Americans rely on Medicare Part D. The program must not be drastically changed until their voices have a chance to be heard.

Sincerely,

Merrill Matthews, Ph.D.
Resident Scholar
Institute for Policy Innovation



INSTITUTE FOR REGULATORY ANALYSIS AND ENGAGEMENT EST. 2021

MEMORANDUM

To: Dr. Meena Seshamani, MD PhD, Director, Centers for Medicare & Medicaid Services
From: Andrew Langer, Chairman, Institute for Regulatory Analysis and Engagement
Date: April 14, 2023
Re: Comments Regarding Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments, published by CMS on March 15, 2023

Director Seshamani:

The following are the comments of the Institute for Regulatory Analysis and Engagement (IRAE) on the United States Department of Health and Human Services/Centers for Medicare & Medicaid Services' (CMS) Guidance regarding the Medicare Drug Price Negotiation Program, published March 15, 2023 (found online at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>).

IRAE is a non-profit, non-partisan research, education and advocacy organization. Our mission is to inject a common-sense perspective into the regulatory process, to ensure that risks and costs of regulation are fully considered based on sound scientific and economic evidence and to ensure the voices, interests and freedoms of Americans, and especially of small business, are fully represented in the regulatory process and debates. Finally, we work to ensure that regulatory proposals address real problems, that the proposals serve to ameliorate those problems, and, perhaps most-important, that those proposals do not, in fact, make public policy problems worse.

We are especially interested in issues with a fundamental constitutional bearing, as this proposal certainly is. While many regulatory analyses start and end with an underlying statutory framework and how a proposed rule aligns with an agency's obligations under the Administrative Procedure Act, this analysis also discusses how CMS' proposed guidance has further constitutional implications.

It is our opinion that the Guidance offered by CMS does precisely that—it fails to ameliorate the problems it is supposed to address, instead will making matters far worse, while at the same time having constitutional implications.

IRAE offers the following:

- The program forces manufacturers to comply with data-sharing limitations that constitute a clear violation of their First Amendment right to free speech. Additionally, the methodology proposed for determining drug prices is fundamentally flawed. The provisions stipulated in the propose guidance will impose needlessly onerous burdens on U.S. drug manufacturers and ultimately hurt patients.
- According to Section 40.2.2 of the guidance (Data Use Provisions and Limitations), manufacturers would be prohibited from disclosing to the public any information from negotiations with CMS. This includes information about ceiling-price offers, CMS's justification for its offers, or any information derived from the process. This would infringe on the free-speech rights of manufacturers and is at direct odds of open and transparent government.
- CMS proposes onerous, draconian measures to enforce this secrecy. For example, audio and video recordings of conversations between CMS and manufacturers would be prohibited. This completely ignores the reality of corporate operations in the modern age, where digital records are a normal part of interoffice communication.
- Similarly, CMS places an unreasonable demand on manufacturers by requiring that they certify within 30 days the destruction of all information from the negotiation period -- including the manufacturer's own written notes and emails -- should a drug or biologic no longer qualify as a selected drug.

It should also be noted that Section 40.2.2 would almost certainly be rejected by the courts. The Supreme Court has consistently and correctly struck down prior restraints of speech. IRAE finds it interesting that this is yet another rulemaking in 2023 alone that has the Biden Administration at odds with the First Amendment, and the second time in as many months that IRAE has expressed such concerns with a subdivision of the Department of Health and Human Services.

Which begs the question: why is this administration, why is this federal agency, so focused on impinging on the First Amendment rights of American citizens?

What the guidance seems to require is also in conflict with the Freedom of Information Act and the Biden administration's state transparency principles. While the information that the government would presumably accrue during the negotiation period would be subject to FOIA, manufacturers would be compelled to destroy the very same information and would be prohibited from sharing it with the public.

America's pharmaceutical industry relies on a thriving, collaborative exchange of ideas with scientists, lab workers, patients, and government regulators. Left unamended, Section 40.2.2 will

handicap this exchange of ideas. By prohibiting manufacturers from sharing information about the negotiation process, CMS prevents them from pointing out flaws or methodological problems and educating other manufacturers and stakeholders.

We also have serious concerns regarding how CMS plans on setting maximum fair prices of selected drugs and biologics. According to Section 60.3, Methodology for Developing an Initial Offer, CMS will develop offers based on similar "therapeutic alternatives" for the selected drug and rely on the alternative's net price and average sales price (based on Medicare Part D) to determine a starting point. This is wholly inappropriate, as comparing one drug to a "similar" therapeutic is bound to lead to clinically unsuitable results, given the broad range of unique needs and preferences of patients.

CMS must consider the chilling effect that Section 40.2.2, Date Use Provisions and Limitations, will have on the U.S. drug manufacturing industry, and to eliminate any component of this section that would infringe upon the constitutional First Amendment rights of manufacturers. We also urge CMS to propose a more sensible and accurate method for determining drug pricing.

Without significant revisions, the Drug Price Negotiation Program will throttle, not promote, innovation.

Conclusion

This proposal is bad policy. It fails to address the underlying problem it is trying to solve, will most-likely make that problem worse, and at the same time has serious implications for federal freedom of information law generally and the First Amendment to the Constitution of the United States.

CMS should withdraw this proposal and rework it entirely.

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April 14, 2023

Sent electronically to IRAREbateandNegotiation@cms.hhs.gov

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
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Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Deputy Administrator Seshamani,

Thank you for this opportunity to comment on the Initial
Memorandum for Implementation of the Medicare Drug Price
Negotiation Program.

All Americans share the goals of reducing the costs of healthcare, in
particular, the cost of drugs, while preserving access to the life-
extending and often life-saving benefits of the drugs that treat
cancer, heart disease, Alzheimer's, autoimmune conditions, and so
many other lethal diseases.

We applaud many aspects of the Inflation Reduction Act that will
cap out-of-pocket costs, eliminate cost-sharing for vaccines, and
make insulin much more affordable for patients.

ICAN, International Cancer Advocacy Network, is a 501(c)(3) non-
profit organization that connects Stage IV cancer patients to clinical
trials, cutting-edge treatments at our leading academic centers,
second opinions, and other services that patients dealing with the
most serious stage of cancer require. Since our founding in 1996, we
have helped over 17,500 patients in all 50 states and 72 foreign
countries. Additionally, ICAN started the Exon 20 Group in 2017 to
aid patients fighting two rare genetic mutations that are particularly
associated with very lethal lung cancer.

In short, we deal every day with patients who are dependent on the
drug discovery pipeline to extend, and in an increasing number of

cases, save their lives. Our main focus when it comes to matters of legislation and regulation, whether on the state or federal level, is thus on protecting that pipeline. We wish to offer an actual “in-the-trenches” perspective on these issues.

There are many ways that the Medicare Drug Price Negotiation Program can be improved. In particular, we wish to associate ourselves with the detailed comments and very thoughtful recommendations of the Personalized Medicine Coalition (PMC), the Partnership to Improve Patient Care (PIPC), the Council for Affordable Health Coverage (CAHC), the Haystack Project, and the Chronic Care Policy Alliance (CCPA).

We will focus these comments on the drug discovery pipeline and continued access to the widest possible choice of drugs, both those currently available, and those that will be available in the future. Every single person—including all those reviewing this and the many other comments on these issues—has a very personal stake in protecting that pipeline and that access.

Ultimately, there are two main forces that will drive down costs: 1) the drug discovery pipeline, and 2) the increasing ability to tailor treatments to the specific person—personalized medicine. One has only to think of the impact on healthcare costs of an effective treatment for Alzheimer’s, or a long-term cure for one of the many forms of cancer.

We wish to emphasize the following:

1) Incorporating the Patient Voice: CMS should create much greater opportunities to incorporate the patient voice in the development of the program and the decisions that will be made regarding drugs. This includes such proposals as regional roundtables and participation via teleconference to include those who may not be able to travel to Washington, D.C., or a regional roundtable, due either to cost, physical disability, or health limitations from the condition or treatment.

2) Extend the Time for Feedback: CMS should extend the amount of time for feedback by stakeholders once the list of selected drugs is announced. 30 days is simply too short to receive the kind of serious feedback that is essential for this process (see the above point for ways to improve feedback).

3) Remove Disincentives for Investment: The distinction between nine years before price negotiations/price setting for small molecule drugs (e.g. pills and tablets) versus 13 years for large molecule drugs (e.g., biologics) will inevitably distort the market from initial investment through decisions made after approval. This will have an almost certain negative impact on investment in drug discovery. Biologics are wonderful and we hope for many more discoveries in that area, but what should determine investment decisions is the science and the promise of a drug rather than the arbitrary class a drug falls into.

Additionally, there are many decisions made after a drug is approved that will be negatively affected by these arbitrary timelines. Currently, there are obvious incentives to invest in research to find additional uses for a drug. What incentive will there be under these timelines? Indeed, they will rapidly decline every year after approval. Thus, there will inevitably be fewer drugs being discovered and even fewer of those will be developed. Patients will suffer on both fronts.

We are aware that removing these disincentives for investment will require legislation to correct the problem. However, CMS can certainly recommend such changes to Congress.

4) **Using Research:** There are three critical areas that CMS should consider when implementing the IRA:

a) Avoiding Being Misled by the Wrong Average: Just as you would not judge a cancer cure by merging the population of cancer patients and those of another disease, so it is a mistake to rely on the average of the progression-free survival statistics even for a specific cancer (and this applies to any other disease). Any process that does not take into account “exceptional responders” will be fundamentally flawed and will cause real, measurable damage to the patients who are being helped by a drug.

b) Incorporate Real World Evidence (RWE): Similar to the point above, a drug should be continually re-evaluated to see the value of a drug to patient outcomes in multiple sub-populations (e.g., ethnicities and gender, but also other factors such as comorbidities).

c) Ensure that Quality-Adjusted-Life Years (QALYs) are not used when evaluating drugs: We are aware that the law prevents direct use of QALYs, but CMS should make it explicitly clear that QALYs will not be used in any manner —*including indirectly*.

The advances in treatments for cancer, heart disease, autoimmune diseases, and many other serious or fatal conditions over the past 50 years have been astonishing. Most of these advances were due to drug discovery. It is the United States, as all statistics make clear, that has led the way in most of these fields, and has done majority of drug discovery throughout the world. It is these continued breakthroughs that will lead to not only reductions in healthcare costs, and reductions in health disparities for underserved populations, but also, and most importantly, to extended life with a higher quality of life for millions of people in the United States and around the world.

We ask you to keep those people in mind as you make these critical decisions.

Please do not hesitate to contact me at marcia@askican.org or (602) 618-0183 if you need any additional information.

Thank you for your consideration.

Respectfully submitted,



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Dear Dr. Seshamani,

ISPOR – the professional society for health economics and outcomes research (HEOR) - is pleased to respond on behalf of its membership to your consultation “**Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments.**”

ISPOR is a scientific and educational society with many of its members engaged in evaluation of health technologies, including pharmaceuticals, medical devices, and other interventions. Established in 1995, ISPOR is a not-for-profit organization and the leading source for scientific conferences, peer-reviewed and MEDLINE®-indexed publications, good practices guidance, education, collaboration, and tools/resources in the HEOR field. We have a large membership living and working in 110 countries globally, across a range of disciplines, including health economics, epidemiology, public health, pharmaceutical administration, psychology, statistics, medicine, and more, from a variety of stakeholder perspectives, such as the life sciences industry, academia, research organizations, payers, patient groups, government, and health technology assessment bodies. The research and educational offerings presented at our conferences and in our journals are relevant to many of the issues and questions raised in this request for information.

The response to this consultation was led by the Policy Outlook Committee of our most senior advisory body, the Health Science Policy Council. To engage our membership, we created a survey where their comments on different sections of the Memorandum could be recorded. We recognize that the Inflation Reduction Act (IRA) gives Secretary the option to consider a variety of different factors as part of the negotiation. Most of our members would strongly support consideration of “[t]he extent to which such drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives.” We have less consensus on the other suggested factors, but we will leave to it those individual members to submit their detailed comments on those. We chose to provide comments in the areas most related to our scientific expertise, which is represented in part by an extensive set of Good Practices and similar reports (<https://www.ispor.org/heor-resources/good-practices>). Our comments are summarized in six major points below.

1. **CMS definition of unmet need.** Section 1194(e)(2) of the Act directs CMS to consider evidence about alternative treatments to the selected drug, as available, including, “the extent to which the selected drug and the therapeutic alternatives to the drug address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy.” However, in the memorandum (p. 51), it is stated that “CMS will consider whether the selected drug fills an unmet medical need, which CMS intends to define as treating a disease or condition in cases where very limited or no other treatment options exist.”

We believe that this narrower interpretation of unmet need, while perhaps easier to identify and implement, may disadvantage some therapies where, despite available treatment and interventional options, a substantial burden of disease remains and significant healthcare (therapeutic, diagnostic, preventative) innovations are needed. Heart disease and cancer are still the leading causes of mortality¹ despite many treatments that improve outcomes. The actual burden of disease includes both direct and indirect factors beyond mortality, including loss of functionality, pain, mental illness, and sensory deficits (ie, quality of life deficits, as well as effects on caregivers, etc). In addition, the negative impact of these diseases on quality of life can be measured via disease-specific utilities, which are readily available² but absent from the definition of unmet need. Neurological diseases are additional examples where treatments may exist, such as for Parkinson's disease, but the unmet medical need is still high, and the value of addressing such unmet need should be clearly reflected in the Maximum Fair Price (MFP). Most new products are supported by burden of illness studies and updated research should support MFP negotiation.

2. **Comparative effectiveness.** “Comparative effectiveness of the selected drug and its therapeutic alternatives” is clearly a key consideration in MFP determination and we fully support CMS in its plan to use real-world evidence (RWE) in this area. We would like to make a few points here:
- 1) RWE will complement randomized clinical trial (RCT) data, clinical guidance, and expert consultation (including manufacturers and patients) in determining the most relevant therapeutic alternatives. RWE can indicate which alternatives are most used in general, as well as in different clinical situations (often including different indications) or key subpopulations.
 - 2) While recognizing the recent guidance from the FDA and other bodies relating to RWE, evaluating the quality of the research generating RWE can also be informed by a number of ISPOR Good Practices reports on comparative effectiveness research (CER), including these topics:
 - i. Defining, reporting, and interpreting³
 - ii. Bias and confounding in the design⁴
 - iii. Causal inference⁵
 - iv. Transparency⁶

¹ Xu JQ MS, Kochanek KD, Arias E. Mortality in the United States, 2021, NCHS Data Brief, no 456. In: National Center for Health Statistics, ed. Hyattsville, MD 2022.

² Cost-Effectiveness Analysis (CEA) Registry. The Center for the Evaluation of Value and Risk in Health 2023.
<https://cear.tuftsmedicalcenter.org/>.

³ Berger ML, Mamdani M, Atkins D, Johnson ML. Good research practices for comparative effectiveness research: defining, reporting and interpreting nonrandomized studies of treatment effects using secondary data sources: the ISPOR Good Research Practices for Retrospective Database Analysis Task Force Report—part I. *Value Health*. 2009;12(8):1044-1052.

⁴ Cox E, Martin BC, Van Staa T, Garbe E, Siebert U, Johnson ML. Good research practices for comparative effectiveness research: approaches to mitigate bias and confounding in the design of non-randomized studies of treatment effects using secondary data sources: the ISPOR Good Research Practices for Retrospective Database Analysis Task Force—part II. *Value Health*. 2009;12(8):1053-1061.

⁵ Johnson ML, Crown W, Martin BC, Dormuth CR, Siebert U. Good research practices for comparative effectiveness research: analytic methods to improve causal inference from nonrandomized studies of treatment effects using secondary data sources: the ISPOR Good Research Practices for Retrospective Database Analysis Task Force Report—Part III. *Value Health*. 2009;12(8):1062-1073.

⁶ Berger ML, Sox H, Willke RJ, et al. Good practices for real-world data studies of treatment and/or comparative effectiveness: Recommendations from the joint ISPOR-ISPE Special Task Force on real-world evidence in health care decision making. *Pharmacoepidemiol Drug Saf*. 2017;26(9):1033-1039.

- v. Replicability (joint with the International Society for Pharmacoepidemiology [ISPE])⁷
- vi. Assessing relevance and credibility⁸

3) Different studies will yield different results, so evidence synthesis is likely to be necessary to generate a primary estimate of the difference in effect (with the recognition that uncertainty is present). Methods such as network meta-analysis and indirect treatment comparisons may be important here, and ISPOR has also created several Good Practices Reports on this topic:

- i. Interpretation⁹
- ii. Conduct¹⁰
- iii. Assessing relevance and credibility¹¹

3. **Value considerations.** Translating comparative effectiveness to fair pricing involves an assessment of the value of treatment effects, since pricing needs to be fair not only within a disease area, where CER can provide answers, but also across diseases, where CER does not. Value of treatment to patients and society involves several factors, probably most important of which is the clinical benefit per se, but other factors can be important as well. The delineation and estimation of those factors has been described recently by ISPOR¹² and by the Second Panel on Cost-Effectiveness in Health and Medicine,¹³ among others. Factors that are based on value to individuals include severity of disease, insurance value, value of hope, real option value, family spillovers, and others. CMS is well-positioned to also take into account factors that have broader value to society, such as productivity loss/gain, scientific spillovers, health equity, and others noted in ISPOR's "Value Flower" and in the Second Panel's Impact Inventory. While measurement of some of these factors is an evolving science, good progress¹⁴ is being made and it is presently feasible to take many of them into account.

4. **Measuring clinical benefit.** The exact metric for capturing clinical benefit in value calculations that includes not only survival gains but also quality of life improvements, has been a matter of considerable

⁷ Wang SV, Schneeweiss S, Berger ML, et al. Reporting to Improve Reproducibility and Facilitate Validity Assessment for Healthcare Database Studies V1.0. *Pharmacoepidemiol Drug Saf.* 2017;26(9):1018-1032.

⁸ Berger ML, Martin BC, Husereau D, et al. A questionnaire to assess the relevance and credibility of observational studies to inform health care decision making: an ISPOR-AMCP-NPC Good Practice Task Force report. *Value Health.* 2014;17(2):143-156.

⁹ Jansen JP, Fleurence R, Devine B, et al. Interpreting indirect treatment comparisons and network meta-analysis for health-care decision making: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 1. *Value Health.* 2011;14(4):417-428.

¹⁰ Hoaglin DC, Hawkins N, Jansen JP, et al. Conducting indirect-treatment-comparison and network-meta-analysis studies: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 2. *Value Health.* 2011;14(4):429-437.

¹¹ Jansen JP, Trikalinos T, Cappelleri JC, et al. Indirect treatment comparison/network meta-analysis study questionnaire to assess relevance and credibility to inform health care decision making: an ISPOR-AMCP-NPC Good Practice Task Force report. *Value Health.* 2014;17(2):157-173.

¹² Lakdawalla DN, Doshi JA, Garrison LP, Jr., Phelps CE, Basu A, Danzon PM. Defining Elements of Value in Health Care-A Health Economics Approach: An ISPOR Special Task Force Report [3]. *Value Health.* 2018;21(2):131-139.

¹³ Neumann PJ, Ganiats TG, Russell LB, Sanders GD, Siegel JE. *Second Panel on Cost-Effectiveness in Health and Medicine.* Oxford University Press; 2016.

¹⁴ Neumann PJ, Garrison LP, Willke RJ. The History and Future of the "ISPOR Value Flower": Addressing Limitations of Conventional Cost-Effectiveness Analysis. *Value Health.* 2022;25(4):558-565.

debate.¹⁵ The IRA legislation forbids the use of the most standard measure, quality-adjusted life-years (QALYs), to the extent it gives relatively lower value to the extension of life of older, disabled, or terminally individuals. We do not believe that in most cases use of QALYs will disadvantage those groups since incremental QALY gain between treatments is the actual benefit measure and typically those groups will be represented in both treatment and comparator groups. The focus on treatment-based gains in quality of life is in fact generally more likely to benefit these groups since they tend to have lower quality of life ratings prior to treatment.

However, in cases where the value of treatment that extends survival in an older, disabled, or terminally ill population is being compared to the value of treatment to a more general population, alternative measures can be used such as equal value of Life Years Gained (evLYG),¹⁶ health years in total (HYT),¹⁷ and the generalized risk-adjusted QALY (GRA-QALY)¹⁸. Extended discussions of the use of QALYs relative to these alternative measures can be found in recent or forthcoming articles.^{19,20,21} In short, we recommend that CMS work with ISPOR and other expert groups in this area to settle on the most feasible approach to including both survival and quality of life gains in a clinical benefit measure for use in value calculations.

5. **Qualitative approach.** To provide some structure to the “qualitative” approach that CMS intends to use to adjust the MFP starting point for other clinical and value-based considerations, we recommend two considerations.

First, it is useful to have a single value construct to aggregate different factors influencing the value of treatment. The standard cost/QALY metric used by many countries and other groups does not easily capture all value elements and is of course based on the QALY measure. An ISPOR task force on value assessment suggested several such aggregate measures.²² One approach is a specific deliberative process called multi-criteria decision analysis (MCDA) that results in a single value construct; ISPOR has

¹⁵ Owerhohle S. Could a fight over cost-effectiveness upend Medicare drug price negotiation before it's begun? *Stat.* 2023. <https://www.statnews.com/2023/03/28/qaly-medicare-negotiation-drugs/>. Accessed April 12, 2023.

¹⁶ Institute for Clinical and Economic Review. Cost-Effectiveness, the QALY, and the evLYG. <https://icer.org/our-approach/methods-process/cost-effectiveness-the-qaly-and-the-evlyg/>. Published 2023. Accessed April 12, 2023.

¹⁷ Basu A, Carlson J, Veenstra D. Health Years in Total: A New Health Objective Function for Cost-Effectiveness Analysis. *Value Health.* 2020;23(1):96-103.

¹⁸ Lakdawalla DN, Phelps CE. Health technology assessment with risk aversion in health. *J Health Econ.* 2020;72:102346.

¹⁹ Cohen JT, Neumann PJ, Ollendorf DA. The much-maligned ‘quality-adjusted life year’ is a vital tool for health care policy [Opinion]. *Stat.* 2023. <https://www.statnews.com/2023/03/22/the-much-maligned-quality-adjusted-life-year-is-a-vital-tool-for-health-care-policy/>. Published March 22. Accessed April 14, 2023.

²⁰ Shafrin J LD, Doshi JA, et al. A Strategy for Value-Based Drug Pricing Under the Inflation Reduction Act. In: Affairs H, ed. *Health Affairs Forefront.* Forthcoming.

²¹ Sullivan SD LD, Devine B. Alternatives to the QALY for Comparative Effectiveness Research. In: Affairs H, ed. *Health Affairs Forefront.* Forthcoming.

²² Phelps CE, Lakdawalla DN, Basu A, Drummond MF, Towse A, Danzon PM. Approaches to Aggregation and Decision Making-A Health Economics Approach: An ISPOR Special Task Force Report [5]. *Value Health.* 2018;21(2):146-154.

issued a pair of Task Force reports^{23,24} that describe how MCDA works. In this case it would involve having a group of educated stakeholders weigh relevant measures, including a clinical benefit measure but not necessarily the QALY, in a process that results in a single value measurement. MCDA can be conducted in a way that uses different value elements in different cases but can be comparable across cases as long as a common clinical benefit measure is employed.

Second, the broader qualitative process CMS intends to use can be informed by, or could directly use, a deliberative process as well, which has been described for use in health technology assessment (HTA).²⁵ Deliberative processes for HTA are intended to facilitate participatory decision making, using discussion and open dialogue between stakeholders. They are a specific instance of the type of process that employs “accountability for reasonableness”²⁶ as a basis for establishing fairness. We encourage CMS to consider such an approach.

6. **General process considerations.** This initial year involves some relatively short timelines that are necessary due to the legislation and do not realistically offer time for deliberative processes and may limit meaningful stakeholder engagement. We encourage CMS to consider extending timelines for future years to facilitate transparency in these assessment methods (preferably including a memorandum detailing the qualitative process that becomes used) and allow for more extensive engagement and deliberation. We also encourage CMS to consider adapting their guidance for this process based on learnings from the initial implementation experience.

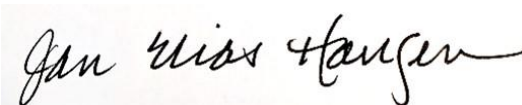
We thank CMS for the opportunity to comment on this consultation; if you have questions about any of these comments, please contact our Chief Science Officer, Richard Willke, at rwillke@ispor.org.

We look forward to working with CMS throughout the implementation of the program. We know this will be a multiyear process and that approaches and methods may change along the way. We welcome the opportunity for further discussion about the considerations in this response and to engage in additional consultations.

Sincerely,



Robert Abbott
CEO & Executive Director
ISPOR



Jan Elias Hansen, PhD
President 2022-2023, ISPOR
Vice President, Evidence for Access, Genentech

²³ Marsh K, IJzerman M, Thokala P, et al. Multiple Criteria Decision Analysis for Health Care Decision Making--Emerging Good Practices: Report 2 of the ISPOR MCDA Emerging Good Practices Task Force. *Value Health*. 2016;19(2):125-137.

²⁴ Thokala P, Devlin N, Marsh K, et al. Multiple Criteria Decision Analysis for Health Care Decision Making--An Introduction: Report 1 of the ISPOR MCDA Emerging Good Practices Task Force. *Value Health*. 2016;19(1):1-13.

²⁵ Oortwijn W, Husereau D, Abelson J, et al. Designing and Implementing Deliberative Processes for Health Technology Assessment: A Good Practices Report of a Joint HTAi/ISPOR Task Force. *Value Health*. 2022;25(6):869-886.

²⁶ Daniels N. Accountability for reasonableness. *BMJ*. 2000;321(7272):1300-1301.

APPENDIX: ISPOR Task Force and other Reports Referenced in this Document (*numbered as listed in the letter footnotes*)

3. Berger ML, Mamdani M, Atkins D, Johnson ML. Good research practices for comparative effectiveness research: defining, reporting and interpreting nonrandomized studies of treatment effects using secondary data sources: the ISPOR Good Research Practices for Retrospective Database Analysis Task Force Report—part I. Value Health. 2009;12(8):1044-1052. <https://doi.org/10.1111/j.1524-4733.2009.00600.x>
4. Cox E, Martin BC, Van Staa T, Garbe E, Siebert U, Johnson ML. Good research practices for comparative effectiveness research: approaches to mitigate bias and confounding in the design of non-randomized studies of treatment effects using secondary data sources: the ISPOR Good Research Practices for Retrospective Database Analysis Task Force—part II. Value Health. 2009;12(8):1053-1061. <https://doi.org/10.1111/j.1524-4733.2009.00601.x>
5. Johnson ML, Crown W, Martin BC, Dormuth CR, Siebert U. Good research practices for comparative effectiveness research: analytic methods to improve causal inference from nonrandomized studies of treatment effects using secondary data sources: the ISPOR Good Research Practices for Retrospective Database Analysis Task Force Report--Part III. Value Health. 2009;12(8):1062-1073. <https://doi.org/10.1111/j.1524-4733.2009.00602.x>
6. Berger ML, Sox H, Willke RJ, et al. Good practices for real-world data studies of treatment and/or comparative effectiveness: Recommendations from the joint ISPOR-ISPE Special Task Force on real-world evidence in health care decision making. Pharmacoepidemiol Drug Saf. 2017;26(9):1033-1039 <https://doi.org/10.1002/pds.4297>
7. Wang SV, Schneeweiss S, Berger ML, et al. Reporting to Improve Reproducibility and Facilitate Validity Assessment for Healthcare Database Studies V1.0. Pharmacoepidemiol Drug Saf. 2017;26(9):1018-1032. <https://doi.org/10.1002/pds.4295>
8. Berger ML, Martin BC, Husereau D, et al. A questionnaire to assess the relevance and credibility of observational studies to inform health care decision making: an ISPOR-AMCP-NPC Good Practice Task Force report. Value Health. 2014;17(2):143-156. <https://doi.org/10.1016/j.jval.2013.12.011>
9. Jansen JP, Fleurence R, Devine B, et al. Interpreting indirect treatment comparisons and network meta-analysis for health-care decision making: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 1. Value Health. 2011;14(4):417-428. <https://doi.org/10.1016/j.jval.2011.04.002>
10. Hoaglin DC, Hawkins N, Jansen JP, et al. Conducting indirect-treatment-comparison and network-meta-analysis studies: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 2. Value Health. 2011;14(4):429-437. <https://doi.org/10.1016/j.jval.2011.01.011>
11. Jansen JP, Trikalinos T, Cappelleri JC, et al. Indirect treatment comparison/network meta-analysis study questionnaire to assess relevance and credibility to inform health care decision making: an ISPOR-AMCP-

NPC Good Practice Task Force report. Value Health. 2014;17(2):157-173.
<https://doi.org/10.1016/j.jval.2014.01.004>.

12. Lakdawalla DN, Doshi JA, Garrison LP, Jr., Phelps CE, Basu A, Danzon PM. Defining Elements of Value in Health Care-A Health Economics Approach: An ISPOR Special Task Force Report [3]. Value Health. 2018;21(2):131-139. <https://doi.org/10.1016/j.jval.2014.01.004>.

14. Neumann PJ, Garrison LP, Willke RJ. The History and Future of the "ISPOR Value Flower": Addressing Limitations of Conventional Cost-Effectiveness Analysis. Value Health. 2022;25(4):558-565.
<https://doi.org/10.1016/j.jval.2022.01.010>

22. Phelps CE, Lakdawalla DN, Basu A, Drummond MF, Towse A, Danzon PM. Approaches to Aggregation and Decision Making-A Health Economics Approach: An ISPOR Special Task Force Report [5]. Value Health. 2018;21(2):146-154. <https://doi.org/10.1016/j.jval.2017.12.010>

23. Marsh K, IJzerman M, Thokala P, et al. Multiple Criteria Decision Analysis for Health Care Decision Making--Emerging Good Practices: Report 2 of the ISPOR MCDA Emerging Good Practices Task Force. Value Health. 2016;19(2):125-137. <https://doi.org/10.1016/j.jval.2015.12.016>

24. Thokala P, Devlin N, Marsh K, et al. Multiple Criteria Decision Analysis for Health Care Decision Making--An Introduction: Report 1 of the ISPOR MCDA Emerging Good Practices Task Force. Value Health. 2016;19(1):1-13. <https://doi.org/10.1016/j.jval.2015.12.003>

25. Oortwijn W, Husereau D, Abelson J, et al. Designing and Implementing Deliberative Processes for Health Technology Assessment: A Good Practices Report of a Joint HTAi/ISPOR Task Force. Value Health. 2022;25(6):869-886. <https://doi.org/10.1016/j.jval.2022.03.018>.



April 14, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
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Department of Health and Human Services
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IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Jnana Therapeutics appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023.

I am the CEO of Jnana, a small biotech company focused on developing new oral medicines for diseases where patients are in urgent need of better treatments. The company was founded in 2017, is based in Boston, Massachusetts, and currently has about 85 employees. Within Jnana, we have built an innovative platform for discovering small molecules that modulate previously undruggable targets. We are advancing first-in-class therapies to treat rare diseases and autoimmune & inflammatory diseases. I am writing because of our concern that our ability to maximize the benefit to patients from the new medicines we are developing may be negatively impacted by CMS's implementation of the Drug Price Negotiation Program.

Our concerns:

About 18,000 people in the U.S. are living with the rare disease phenylketonuria (PKU), with most inadequately treated. Our clinical candidate JNT-517, currently in a Phase 1 clinical trial, is a potential new oral medicine for treating PKU that may address much of this unmet medical need. The mechanism by which our clinical candidate operates might also provide an effective approach for treating more rare metabolic diseases such as Maple Syrup Urine Disease, where patients currently have no therapies.

We are now carefully considering whether the loss of exclusion from the CMS Negotiation Program a second rare disease indication might trigger impacts our potential plans to explore additional rare disease indications beyond PKU with JNT-517, given the restrictive criteria for exclusion requiring a drug product be approved for "only one rare disease or condition".

Implementation of the IRA might also impact other programs in our pipeline. Conducting clinical trials in common autoimmune & inflammatory diseases, where patients often have multiple immune pathways dysregulated and the disease is heterogeneous patient to patient, takes a substantial amount of time and funding and carries significant risk. Biotech companies like Jnana often initially test an innovative medicine in a rare immune disease where one of these immune pathways is dysregulated and the disease is less heterogeneous with the aim of most efficiently achieving clinical proof-of-concept and advancing the new medicine to patients.



With our platform, we have discovered a potential first-in-class medicine that may help treat both rare and common autoimmune & inflammatory diseases. Because eligibility for selection for the Negotiation Program occurs only 7 years following the first drug product approval, we may not be able to pursue the optimal drug development route if this route involves initial clinical testing and approval in a rare immune disease.

What can be done to mitigate negative impact on the development of innovative medicines?

We strongly urge CMS to support legislation: 1) extending the Initial Price Applicability for drug products, which is currently 7 years following approval, to the same as biological products, which is currently 11 years following licensure; and 2) eliminating the overly restrictive qualifying criteria for the orphan drug exclusion to enable any medicine only approved for orphan indications to qualify for the exclusion. These changes would incentivize investors to support biotech companies to develop the best possible medicines for the most patients, irrespective of the modality of the medicine, and therefore serve the best interest of patients.

In the absence of such changes in legislation, we urge CMS to start the selection clock on the date a drug product loses its eligibility for the orphan drug exclusion. We further urge CMS to set the maximum fair price under the Negotiation Program at the ceiling price for any drug product until 11 years following approval (the first year of Initial Price Applicability for biological products). We believe these changes are important to better support orphan drug development and the development of innovative medicines more broadly.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to patients from fewer innovative medicines is minimized. Please contact me at jkotz@jnanatx.com if you have any questions regarding our comments.

Sincerely,

A handwritten signature in black ink that reads "Joanne D Kotz". The signature is fluid and cursive, with the first letters of each word being capitalized.

Joanne D Kotz, Ph.D.
Cofounder and CEO
Jnana Therapeutics

April 14, 2023

VIA Electronic Filing – IRAREbateandNegotiation@cms.hhs.gov

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
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Attn: PO Box 8016

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Seshamani:

On behalf of Johnson & Johnson (J&J) we submit the following comments in response to the Centers for Medicare & Medicaid Services' (CMS, the Agency) *Medicare Drug Price Negotiation Program (Program or the Program): Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (Guidance or the Guidance).¹ J&J is the world's most comprehensive and broadly-based manufacturer of healthcare products for pharmaceutical, medical devices, and diagnostics markets. For nearly 130 years, we have led the way in innovation and are continuing this heritage today by bringing important new pharmaceutical products to market in a range of therapeutic areas on behalf of all our current and future patients, including Medicare, Medicaid, and Marketplace beneficiaries. We are engaged members of BIO and PhRMA and endorse their comments also submitted in response to this Guidance while providing further input below.

J&J has serious concerns about the Guidance which will require significant engagement and resolution with manufacturers before Program implementation. As the largest healthcare company in the world, and a leading manufacturer of life-changing therapeutics within the life sciences, we are deeply concerned about the far-reaching impacts of the *Inflation Reduction Act of 2022 (IRA)* on biopharmaceutical innovation. The policies and unworkable operational complexity advanced throughout the Guidance only further increase our concerns regarding the impact this Program will have on current and future beneficiaries.

We are deeply troubled that the Guidance does not address critical priorities on which we sought collective alignment with the Agency since the passage of the IRA. Specifically, our core principles are to advance and promote program operational feasibility and workability, program integrity measures to preserve biopharmaceutical innovation for future beneficiaries, data access and transparency and the assurance of a positive beneficiary impact. Upholding these principles is critical for manufacturers faced with limited opportunity within the confines of the IRA price-setting system masquerading as

¹ Available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>

“negotiation.” In a true negotiation, all parties to the Agreement would have clear standards that guarantee a consistent methodology and process, transparent access to data, the ability to interpret and defend submitted data, and fundamental rights to due process.

The Guidance was a genuine opportunity to offer the primary party to the “negotiation” predictability and transparency throughout the Program. In place, the Guidance lacks sufficient clarity in describing the Agency’s intended approach and methodology, restricts opportunities for meaningful input (with certain sections limiting comment and response altogether), strictly limits our Agency engagement, proposes ill-defined standards that do not approximate any form of a “negotiation” and creates significant uncertainty about the future of the Program’s policies and operations, all of which will lead to meaningful consequences for the Medicare beneficiaries of today and tomorrow.

We urge CMS to significantly increase their engagement with key stakeholders, extend the timelines for public comments and re-work a substantial portion of the Guidance to align with the statutory mandate of a predictable Program that employs consistent processes and methodologies. We are also aligned with the comments submitted by PhRMA regarding the applicability of section 1871 of the Social Security Act to the Guidance.

With recognition of our significant concerns, we urge CMS to *prioritize* the following issues within the updated Guidance:

- CMS’ definition of a qualified single source drug (SSD) as proposed in the Guidance departs from well-established statutory definitions and we urge CMS to consider the significant unintended consequences for beneficiaries and innovation with adopting the definition as proposed;
- Set the Maximum Fair Price (MFP) for selected drugs at the ceiling price for all Medicare Part D medicines for the first ‘initial price applicability year’ (IPAY 2026) to advance a more reasonable timeline for Program implementation and to allow for the development of greater Agency experience and expertise;
- Effectuate the MFP via a data-driven, retrospective discount model facilitated by a Third-Party Administrator (TPA);
- Revise the Guidance to prevent duplicate MFP-340B discounts as required under law;
- Adopt a simplified application of the MFP specific to each dosage form and strength;
- Adopt the definition of “manufacturer” as described in Statute at 1847(c)(6)(A);
- Explicitly prioritize the impact to Medicare beneficiary lives, health outcomes, and society for selected drugs in evidence review;
- Request CMS issue proposed guidance, with comment opportunity, about the interaction between the Program and the Part B inflation rebate program ahead of 2028; and
- Request CMS coordinate with the Food and Drug Administration (FDA) in the further development of Guidance and throughout the implementation of the IRA

Our complete recommendations are below.

IDENTIFICATION OF SELECTED DRUGS FOR INITIAL PRICE APPLICABILITY YEAR 2026 (Section 30)

The Agency's approach to Section 30 will lead to unintended consequences for patients, including Medicare beneficiaries and beyond, through its threat to innovation of new drugs and further innovation of existing drugs.

J&J recognizes that CMS is not accepting comments to Section 30 and has issued this section as "final." However, we anticipate there will be significant consequences of the approach CMS sets forth in Section 30 through its departure from longstanding and well-established definitions and interpretations of a single source drug.

There is a high likelihood that this departure will lead to additional unintended consequences that we cannot yet identify. The IRA is a complicated and convoluted statute. Under these circumstances and given the magnitude of the impact to Medicare beneficiaries, as well as other patients, a measured approach would be more prudent, and would still align to statutory requirements and timelines. This would mitigate unintended consequences apt to occur under such rushed deadlines.

Below, we highlight a few particulars of concern.

A. The Agency's Definition of a Qualified SSD Departs from Well-Established Statutory Definitions.

The Agency's definition of a "qualified" SSD departs from well-established statutory definitions and interpretations of a single source drug (SSD). While the statute added 'qualifiers,' it did not redefine SSDs. The qualifiers should be interpreted as limiting which SSDs are eligible to be negotiated and subsequently selected by CMS for negotiation. This is the only approach that harmonizes with other Federal health care law and operational realities.

The plain language of the IRA states what drugs are potentially subject to the compulsory discounting mechanism. IRA § 1192(e). The statute uses the "term of art" "single source drug," found throughout multiple prior statutes, to identify and limit the drugs subject to the mechanism. *Id.*; See 42 U.S.C. § 1396r-8(k)(7)(A)(iv)) (defining "single source drug" as "a covered outpatient drug ...which is produced or distributed under a new drug application (NDA) approved by the Food and Drug Administration"); 42 U.S.C. § 1395w-3a(c)(6)(D) (defining "single source drug or biological" as "a biological or a drug which is not a multiple source drug and which is produced or distributed under a NDA approved by the Food and Drug Administration...").

That "term of art" is reinforced by the plain language of § 1992(e) itself. A "drug" is defined by referencing an "approv[al]" under Section 505(c) of the Federal Food, Drug, and Cosmetic Act—the FDCA provisions under which single source drugs obtain approval through an NDA. A "biologic" subject to § 1192(e) similarly must be "licensed under section 351(a) of the Public Health Service Act" under which a single source biologic obtains approval through a Biologics License Application (BLA). Section 1992(e) refers to "qualifying"¹ single source drug to then denote that subset of "single source drugs" that meet the other plain language limitations of the statute.²

Multiple provisions within the Act reinforce that § 1192(e) controls what drugs and biologics are and are not subject to the compulsory discounting process. See § 1192(c)(1) ("selected drugs" determined "in

² IRA § 1192(e).

accordance with subsection (i)(2)”), (d)(1) (“negotiation-eligible drug” is “a qualifying single source drug, as defined in subsection (e)”), (d)(1)(B) (“high spend drug is, determined in accordance with subsection (e)(2),...”).

Section 1192(d)(3)(B) references the use of “data that is aggregated across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended-release formulation”. However, that reference to data is not a part of the subsection that defines a “qualifying single source drug.” The plain language of § 1192(d)(3)(B) states that such data is only to be used “[i]n determining whether a qualifying single source drug,” separately determined under subsection (e), “satisfies any of the criteria described in paragraph (1) [regarding negotiation-eligible drugs] or (2) [regarding the “small biotech” exception].”

In other words, the plain language of § 1192(d)(3)(B) states that, once a “qualifying single source drug” has been determined, use of data in accord with § 1192(d)(3)(B) for the specifically, limited purposes delineated there, is appropriate. Those limited purposes only concern the calculation of the “total expenditures” used to identify negotiation eligible drugs or to determine if the small biotech exception applies. But data use for the purpose of determining total expenditures does not function to expand qualified SSDs that are subject to the MFP.

All the above is important because CMS’ definition of a qualified SSD creates unnecessary conflict and complexity with other Federal health care programs. Statutes should be interpreted in a manner compatible with the existing body of law into which the statute will be applied particularly where Congress is aware of existing laws on the same subject when it passes a new law.³ We urge CMS to harmonize the definition of qualified SSDs to other Federal health care programs to which it will be applied. This will better enable more reasonable, efficient, and successful implementation of the IRA.

B. There Will Be a Significant Impact on Incremental Innovation with CMS’ Approach to Defining a qualifying SSD.

If CMS adheres to the approach outlined in the Guidance, there will be unintended consequences. We highlight just a few here.

Most importantly, if CMS’ definition of a qualified SSD was applied to drugs already being marketed, there are clear examples where incremental innovation never would have occurred. We urge CMS to consider that some innovations and continuous improvement vastly enhance product profiles and increase product safety and effectiveness. The value of this innovation is established through commercial payer negotiations which inure to the benefit of government programs through Medicare, Medicaid, VHCA and 340B pricing calculations.

There are clear examples of incremental innovation leading to standard of care, or other much needed benefits by patients. And we should not overlook that today’s innovation leads to tomorrow’s generics.

For example, had the IRA already been in effect, there is a high likelihood that drugs society depends on today for mental health conditions, such as Long Acting Injectables (LAIs), that have become standard of care, may never have been developed. LAIs were developed following initial discovery and approval of certain oral solid dosage forms of the drugs. LAIs have improved patient adherence, reduced overall health

care costs, and lowered societal burden (e.g., reduced risk of incarceration in schizophrenia patients treated with long-acting injectable anti-psychotics).^{3,4,5}

Similarly, considerable continued development and innovation has been undertaken for drugs used to treat HIV. Without this incremental innovation, many patients today would be without therapies to maintain control over their HIV.^{6,7} The disincentives embodied by CMS’ definition of a qualified SSD risk bringing a halt to further innovation of HIV medicines, unless an entirely new active moiety were discovered. And yet, much of the innovation and advancements in HIV has been made from the initial approved drug(s).

As the examples above convey, we believe CMS’ approach is apt to significantly jeopardize future meaningful innovation for beneficiaries. We urge CMS to appreciate that continuous innovation involving drugs approved under an initial NDA enhance product profiles, can increase product safety and effectiveness, as well as patient adherence and can lead to savings with respect to in other health care costs as safety and patient compliance increase.

To summarize, by aggregating qualified SSDs to apply to new NDCs under an NDA or those with the same active moiety/ingredient, CMS further jeopardizes innovation and the harm that the IRA is likely to cause as it will constrain investment of time, resources and effort on incremental innovation that could benefit patients and may become the next standard of care.

C. Creation of an Extra-Statutory “Bona Fide” Marketing Standard

§ 1192(e) states that the presence of an “approved and marketed” generic drug under FDCA § 505(j) or biosimilar under PHS § 351(k) results in the exclusion of the reference product from the definition of a qualified SSD. This is a critically important protection provided to manufacturers that face generic competition and, therefore, already are subject to substantial pricing pressure. In articulating this protection, the plain language of the statute refers to a generic drug or biosimilar that is “marketed.” IRA § 1192(e).

However, the IRA creates a new standard to determine whether a reference drug or biological is excluded from the definition of a qualified SSD and, therefore, protected from the compulsory discounting mechanism. That new standard – not found in the statute – requires “bona fide marketing” of the generic drug or biosimilar.⁸

This change in substantive legal standard, which was not the subject of public comment, is troubling, for several reasons. First CMS has effectively added the phrase “bona fide” to the statute. Second, the standard

³ *Antipsychotic adherence and rehospitalization in schizophrenia patients receiving oral versus long-acting injectable antipsychotics following hospital discharge*. J Manag Care Spec Pharm. 2015;21(9):754-68.

⁴ *Real-World evidence of clinical and economic impact of long-acting injectables versus oral antipsychotics among patients with schizophrenia in the United States: A systematic review and meta-analysis*. CNS Drugs (2021) 35:469-481.

⁵ APA releases new practice guideline on treatment of patients with schizophrenia. <https://www.psychiatry.org/newsroom/news-releases/apa-releases-new-practice-guideline-on-treatment-of-patients-with-schizophrenia>

⁶ Forsythe FS, McGreevey W, Whiteside A, Shah M, Cohen J, Hecht R, Bollinger LA, and Kinghom A. Twenty Years of Antiretroviral Therapy for People Living With HIV: Global Costs, Health Achievements, Economic Benefits. Health Affairs 2019 38:7, 1163-1172

⁷ Cohen MS, and HPTN 052 Study Team. Antiretroviral Therapy for the Prevention of HIV-1 Transmission. N Engl J Med. 2016 Sep 1;375(9):830-9.

⁸ Guidance Section 30.1 at ps. 10

is undefined. Regulated parties are provided no notice as to what CMS believes is “bona fide” marketing and what is not. Indeed, the criteria to be applied are not disclosed. Third, the standard is fundamentally inconsistent with the commercial realities that apply particularly to generic drugs, which are not marketed in the traditional sense.

An extra-statutory “bona fide” marketing standard, applied to generic drugs and biosimilars, undermines the statutory purpose to protect otherwise qualifying single source drugs from the compulsory discounting mechanism. The risk that the application of that standard would render that protection a nullity appears significant. We therefore urge CMS to remove the “bona fide” marketing requirement and apply the statute as written.

D. Orphan Drug Exclusion

The orphan drug community and patient advocates have expressed significant concern about the limited nature of the exclusion from “qualifying single source drugs” for orphan drugs. Under the statute, an orphan drug may only be designated “for one rare disease or condition” under § 526 of the FDCA and only possess an “approved indication (or indications)” for “such diseases or conditions.” *Id.* § 1192(e)(3). The Guidance asserts a position on this exclusion that contracts it even further, beyond the plain language limits of the text chosen by Congress. The effect is to curtail even the limited protection provided by statute. Unfortunately, the unintended consequence of CMS’ decision will be to undermine innovation in therapies designed to assist vulnerable orphan disease patients even more.

Patient advocates and others have expressed serious concerns about the disturbing implications for innovation in orphan disease treatments created by the statute, even as written. This narrow exception will limit the applicability to orphan therapies, even ultra-orphan therapies, subjecting them to the compulsory discounting process and seriously impacting their viability and, therefore, patient access.

CMS’ final Guidance makes matters worse by asserting that it will consider “all dosage forms and strengths and different formulations” of orphan drugs “as described in Section 30.1” of the Guidance in delineating the exception. This means that orphan drugs under separate NDAs and BLAs will be treated by CMS as a single qualified SSD contrary to the plain language of § 1192(e). The consequence of this will be to deny orphan drug protection, even in some of the limited circumstances required by the plain language of § 1192(e)(3). Such an outcome, contrary to the language, structure, and purpose of the orphan drug exclusion, is concerning, given the negative impact on orphan patient access to therapy and innovation in these important disease areas – where that innovation is so desperately needed.

Notwithstanding these concerns, we appreciate CMS’ comment that “CMS is considering whether there are additional actions CMS can take in its implementation” of the compulsory discounting mechanism “to support orphan drug development.”⁹ We believe that there are important steps that CMS can and should take, including limiting the compulsory discounts imposed on orphan drugs selected under the mechanism to the least extensive discount required to otherwise be imposed under the Act.

We note that, in discussing the possibility of supporting orphan drugs, CMS states that it “will consult with FDA, as needed.” By implication, this excludes all other stakeholders – health care practitioners,

⁹ *Id.* at 11

scientists, patients, patient advocates, and manufacturers – from what could and should be an important discussion. We urge CMS to engage on this important topic with all stakeholders, and we would be interested in participating in that effort.

E. Low-Spend Medicare Drug Exclusion

In addition to the qualified SSD issues identified above, CMS, in articulating its position regarding the low spend Medicare drug exclusion, states that it will employ total expenditures consisting of “the total allowed charges, inclusive of beneficiary cost sharing under Part B.” *Id.* at 11. We believe that this conflicts with the plain language of the statute. The Guidance would include sums that will incorrectly increase the calculation of Medicare spend for purposes of applying the exclusion.

As defined in the IRA, the term total expenditures means, with respect to Part D, “the total gross covered prescription drugs costs (as defined in section 1860D-15(b)(3)).” IRA § 1192(c)(5). Title 42 U.S.C. Section 1860D-15(b)(3) in turn, refers to: “with respect to a Part D eligible individual enrolled in a [Part D plan] ..., the costs **incurred** under the plan, not including administrative costs, but including **costs** directly related to the dispensing of covered ... drugs.” *Id.* (emphasis added). For more than 15 years, CMS, by regulation, has stated that these “costs” must be “actually paid costs”, which in our view, is compelled by the statute’s plain language reference to costs “incurred”. 42 C.F.R. § 423.308. Actually, paid costs or costs “incurred” do not include direct and indirect remuneration (DIR), including discounts, rebates, or other price concessions typically received and applied.” 87 Fed. Reg. 79452, 79611 (Dec. 27, 2022). Because CMS has not acknowledged its departure from this longstanding agency practice or adequately justified its change in course, this element of the Guidance is arbitrary and capricious under the Administrative Procedure Act.¹⁰

The Guidance is inconsistent with the plain language of the statute. As noted, the statute requires that only costs “incurred” be considered. Instead, the Guidance purports to use “total allowed charges.”¹¹ CMS’ intention to exclude DIR amounts, which substantially reduce the costs “incurred,” would seriously erode the protection afforded by the low spend exclusion, threatening significant and adverse patient access and innovation impacts. For all these reasons, we urge CMS to consider only costs actually incurred, as directed in the statute and in keeping with established agency precedent.

F. Plasma-Derived Product Exclusion from Qualifying Single Source Drugs (30.1.3)

CMS proposes to refer to “approved product labeling”¹² to determine if products fall within the plasma-derived product exclusion outlined in section 1192(e)(3)(C) of the Act. We urge CMS to strictly adopt the language in accordance with section 1192(e)(3)(C) of the Act.

G. Submitting an Initial Delay Request for Initial Price Applicability Year 2026 (30.3.1.3)

CMS proposes a template in Appendix B of the Guidance as a useful tool in connection with the Biosimilar Manufacturer’s¹³ intent to submit an Initial Delay Request. However, there are inconsistencies in the proposed submission process. For example, the last paragraph on page 74 of the Guidance states that incomplete or late submissions will not be accepted. However, a subsequent paragraph on page 75

¹⁰ See *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 514 (2009).

¹¹ Guidance Section 30.1.3. ps.11

¹² Guidance Section 30.1.3 ps. 11

¹³ Guidance Section 30.3.1 ps. 16

states that late, incomplete, or inaccurate submissions may adversely affect the negotiation, which suggests a delinquent submission will be accepted. This inconsistency is confusing and should be corrected as follows: If the Biosimilar Manufacturer submits an Initial Delay Request that is not timely, complete, and accurate, the submission may adversely affect the Negotiation Program, including the process for selecting drugs for negotiation for initial price applicability year 2026.

REQUIREMENTS FOR MANUFACTURERS OF SELECTED DRUGS (Section 40)

A. Definition of a Manufacturer

Regarding the definition used for manufacturer, J&J recommends that CMS:

1. Adopt the definition for manufacturer outlined in IRA statute at 1847(c)(6)(A). Under this definition, different manufacturers are not aggregated as one primary manufacturer, and secondary manufacturers are eligible to directly enter into agreements with CMS.
2. Consider the FDA product labeler ID in determining the manufacturer of a product to account for scenarios in which the NDA/BLA holder is not the manufacturer responsible for marketing.

Adopt the Definition of Manufacturer Outlined in the Statute

As noted by CMS and outlined in section 1191(c)(1) of the Act, the Negotiation Program statute adopts the definition of “manufacturer” established in section 1847A(c)(6)(A) of the Act and as defined 1927(k)(5). Despite the clear definition for “manufacturer” outlined in statute, CMS indicates its intent to apply different definitions, for Primary Manufacturer and Secondary Manufacturer, which are terms originating from the Medicaid Drug Rebate Program (MDRP) specific to government pricing calculations for Average Manufacturer Price (AMP) and Best Price (BP). Despite their inclusion in this guidance, neither of these terms is referenced in the IRA. These definitions ignore and override the statutorily adopted manufacturer definition, and do not align to the intent of the law.

We are concerned that the conflicting application of terms and definitions could introduce program integrity issues due to these inconsistencies. In contrast with these terms, the “manufacturer” definition that is laid out in the IRA includes “... any entity which is -engaged in production...OR the packaging, repackaging, labeling, relabeling, or distribution of prescription drug products.”¹⁴ This statutory definition conflicts with CMS’ intent to enter into agreements with only Primary Manufacturers, as the statutory definition for “manufacturer” would apply to “Secondary Manufacturers” which CMS intends to deem ineligible for entering into Medicare Price Negotiation Agreements (Agreements). We agree with the statute that CMS should enter into Agreements with Secondary Manufacturers that meet the statutory definition of “manufacturer.” We urge CMS to follow the statute in defining manufacturer to align with the term defined in section 1847A(c)(6)(A) of the SSA.

In its initial guidance, CMS proposes its intent to hold Primary Manufacturers that enter into Agreements with CMS accountable for collecting and reporting necessary information applicable to any Secondary Manufacturer; and ensuring that any Secondary Manufacturer make the MFP available to MFP-eligible individuals, pharmacies, mail order services and other dispensers. J&J strongly opposes this approach which would not be practical or feasible legally or operationally.

¹⁴ 42 U.S.C. 1396r-8(k)(5)

Primary Manufacturers do not have access to the required data and information for unaffiliated Secondary Manufacturers do not have authority or control over a nonaffiliated Secondary Manufacturer’s operations and cannot “ensure” that another manufacturer makes the MFP available, as the IRA does not provide them with the authority to do so. Secondary Manufacturers are under no obligation to provide Primary Manufacturers with proprietary commercial information, certified government pricing information, or other required data and CMS cannot impose liability on one corporate entity related to the activities of an unaffiliated corporate entity. Further, requiring a Secondary Manufacturer to disclose its trade secrets to a Primary Manufacturer would destroy the trade secrets, potentially resulting in an uncompensated taking of the Secondary Manufacturer’s property and other competitive harms.

In many instances, Primary Manufacturers and Secondary manufacturers are distinct and unaffiliated entities. In fact, Primary and Secondary Manufacturers can be direct competitors in a market, and there is no incentive to exchange or provide commercial practices. Moreover, this forced relationship could hinder cross-industry collaboration and have a negative impact on the development of new therapies for patients. We are concerned that sharing the required data across Primary and Secondary Manufacturers could heighten exposure to federal and state antitrust laws due to the sharing of proprietary information. CMS previously responded to similar concerns in its February 2016 Medicaid Program Final Rule in which the Agency agreed not to finalize its proposal regarding the sharing of pricing data between competing manufacturers and recognized the challenges of obtaining pricing information from non-related manufacturers¹⁵. Lastly, even if a Primary Manufacturer were willing to try to compel a Secondary Manufacturer to share the required information for submission, it would require restructuring of contracts and business terms, as well as the establishment of a process to obtain the information, and it would be infeasible to do so in the period provided in the law and the process outlined by CMS.

We ask CMS to revise all proposals which would hold Primary Manufacturers accountable for the submission of data and pricing actions of unaffiliated Secondary Manufacturers, as Primary Manufacturers do not have access to the required data elements for Secondary Manufacturers and do not have the needed control or authority to ensure their compliance.

CMS should use the unique product labeler ID assigned to each establishment by the FDA to better identify Primary Manufacturer instead of reviewing only the holder of NDA/BLA.

We also ask CMS to clarify in its final guidance how it will handle scenarios in which the manufacturer is not the holder of NDA / BLA. For example, CMS outlines that to the extent that more than one entity meets the statutory definition of manufacturer for a selected drug for purposes of initial price applicability year 2026, CMS intends to designate the entity that holds the NDA(s)/BLA(s) for the selected drug to be “the manufacturer” or “Primary Manufacturer.” There are many instances where the NDA holder is not the Primary Manufacturer, including in the case of split licensures or acquisitions. In these cases, the structure of agreements is unique for each arrangement. For example, responsibilities can be divided per indication, jurisdiction, and other factors etc. In some instances, manufacturers may divide responsibilities, for example, with one entity holding the NDA/BLA and the other responsible for market access and pricing. It is not uncommon for an entity to develop the drug and hold the NDA/BLA and then assign marketing responsibilities to an unaffiliated manufacturer who has more expertise in marketing and access.

¹⁵ 81 FR 5169

B.1. Entrance into an Agreement with CMS (40.1)

CMS should provide manufacturers with visibility to, and the opportunity to comment on, the template agreement to allow for a more expedited review following the publication of the list of selected drugs. We request at least 90 days to review and provide comments on the Agreement before CMS' finalization of the template.

CMS proposes to make “reasonable efforts” to make the final text of the Medicare Drug Price Negotiation Agreement (*Agreement*) available to the public before the selected drug list for IPAY 2026 is published¹⁶. CMS stipulates that manufacturers of selected drugs that elect to enter a negotiation agreement with CMS will have five days following publication of the list of selected drugs to provide contact information for the individuals authorized to execute the Agreement and conduct the negotiation. While the statute states that the Agreements for the initial price applicability year (*IPAY*) need to be signed by October 1, 2023, it does not call for a five-day timeline for review. J&J opposes the creation of a new process not defined in statute, specifically if such processes will result in financial penalties for noncompliance, and we urge CMS not to adopt this five-day timeline. We ask CMS to clarify its interpretation of the statute including its resulting authority regarding this five-day timeline, and to further clarify implications of noncompliance with this proposed five-day timeline, including if there are associated penalties.

B.2. Share the Agreement with Manufacturers in Advance to Provide Sufficient Opportunity to Review and Comment

J&J is concerned that there is insufficient opportunity for manufacturers to review and comment on the Agreement prior to signature, as is typical practice for contract review. J&J underscores the importance of providing manufacturers with sufficient time to review and comment on any agreement which would require signature. We recognize that the statute does not afford ample time before the IPAY, and therefore we ask CMS to establish and provide guidance on an error correction process as it relates to the submission of this data, which will be necessary to ensure program integrity.

C. Submission of Data to Inform Negotiation (40.2)

CMS states its intent to require manufacturers to submit required information for the IPAY by October 2, 2023, noting that manufacturers will not be able to submit this data until the Agreement is fully executed. The statute and its resulting authority did not establish such a short timeline, especially if failure to meet this [impossible] time period is under the penalty of excise tax liability. The agency's proposed approach is therefore contrary to law under the Administrative Procedure Act, 5 U.S.C. § 706(2).

CMS can allow for a longer and more flexible period for data submission beyond October 2, 2023. Thirty (30) days (and a single day following execution of the Agreement) to supply the requested information is infeasible for manufacturers. Under the statute, the October 2, 2023, deadline is limited to non-FAMP data, as per section 1193(a)(4). We ask CMS to clarify its authority to establish such a timeline with associated financial penalties and urge the Agency to extend and implement flexibility in such timelines. Further, we ask CMS to establish and provide guidance on an error correction process as it relates to the submission of this data, which will be necessary to ensure program integrity.

C.1. Confidentiality of Proprietary Information (40.2.1)

¹⁶ Guidance Section 40.1 ps. 27

CMS should provide manufacturers the opportunity to review and comment on the explanation of the MFP prior to publication to confirm that no confidential or proprietary information would be improperly disclosed, additionally the Agency must pursue enhanced measures to protect the confidentiality of company data, including the establishment of a pre-disclosure consultation process with manufacturers.

While we appreciate CMS' stated intent to treat certain data elements as proprietary if they cannot be found publicly, J&J is concerned that CMS has not defined how it will safeguard the sensitive information submitted by manufacturers, and what sources of public information it intends to use to determine if the information is proprietary. It is important manufacturers have confidence their proprietary and highly sensitive, confidential business information will be appropriately protected by CMS, and therefore, we ask CMS to provide guidance on what controls and safeguards it will use to protect confidential information that will be shared under the program. Further, we ask CMS to provide guidance on what acceptable sources of public information it will use to determine if data is confidential and proprietary.

Information regarding Non-Federal Average Manufacturer Price (Non-FAMP or NFAMP), research and development costs, production and distribution costs, and revenue and sales volume, among others, is highly sensitive and often meets the definition of a protected trade secret.¹⁷ It would be very damaging to manufacturers if such confidential and proprietary information were disclosed.¹⁸ The statute clearly directs CMS to safeguard confidential information. Information should be maintained in accordance with standard and customary document retention policies. Therefore, we ask CMS to define and implement a confidentiality policy extending beyond existing FOIA protections, to also align with protections included in other federal programs including MDRP¹⁹, 340B²⁰, etc. We note that Exemption 4 of FOIA addresses disclosure of information, but not use, and therefore CMS' intent to adopt a confidentiality policy consistent with existing proprietary information protections such as Exemption 4 of FOIA is not sufficient, as the Agency's confidentiality policy should cover disclosure and use, as described in statute²¹.

We also ask CMS to establish and provide manufacturers with details on robust storage and access controls and safeguards to protect the confidentiality of sensitive information submitted and stored in HPMS, email or Box. Providing these details to manufacturers is foundational, as it is imperative that manufacturers understand and trust these safeguards prior to engaging in the negotiation process if they are expected to disclose sensitive information. In addition, the confidentiality protections should plainly express that the information submitted by manufacturers is submitted only with the intent that it be maintained and treated as highly confidential. It is expressly not being 'voluntarily' provided as that term is at times used in regard to FOIA. For its confidentiality policies, we ask that CMS provide manufacturers the opportunity to review and provide feedback prior to finalization. J&J is aligned with the recommendations outlined by PhRMA in its comment letter specific to CMS' establishment of confidentiality and data security policies.

¹⁷ See Defend Trade Secrets Act, 18 U.S.C. § 1839(3).

¹⁸ See, e.g., H.R. Rep. 114-529 at 2 (2016) (explaining that "[i]n a global economy based on knowledge and innovation, trade secrets constitute some of [a] company's most valuable property"); S. Rep. No. 114-220 at 1 (2016) (trade secrets are "an integral part of the operation, competitive advantage, and financial success of many U.S.-based companies").

¹⁹ SSA § 1927(b)(3)(D): https://www.ssa.gov/OP_Home/ssact/title19/1927.htm

²⁰ Health Res. & Servs. Admin., General Instructions for Completing the Pharmaceutical Pricing Agreement 7 (2019), available at <https://www.hrsa.gov/sites/default/files/hrsa/opa/pharmaceutical-pricing-agreement-example.pdf>

²¹ 45 CFR 5.41

Finally, given the heightened risk of disclosure of confidential information in CMS' publicly available explanation of the MFP, it is important that CMS provide manufacturers with the opportunity to review and raise concerns prior to publication. The ramifications of an inappropriate disclosure of proprietary information in a publicly posted explanation are so significant for manufacturers that an additional level of review is warranted. Indeed, because trade secrets are extinguished when disclosed to the public,²² CMS should adopt additional confidentiality protections regarding its MFP explanations in order to avoid significant questions under the Fifth Amendment's Takings Clause. Therefore, we ask CMS to provide manufacturers the opportunity to review and comment on the explanation of the MFP prior to publication to confirm that no confidential or proprietary information would be disclosed.

C.2. Data Use Provisions and Limitations (40.2.2)

CMS proposes a data destruction policy which would require the Primary Manufacturer to destroy all information received during the negotiation period from CMS within 30 days of a determination by CMS that the drug or biologic no longer qualifies as a selected drug. J&J does not support this policy which on its face has no direct impact on CMS' ability to achieve an appropriate MFP and undermines transparency. In principle, this policy contrasts with general business operations, internal controls, and accounting practices. We are concerned that this unilateral and onerous data limitation requirement solely on manufacturers will undermine the rights of manufacturers including related to the First Amendment and erodes the spirit of negotiation intended by Congress. J&J is concerned with this proposal and asks CMS to clarify how it relates to the Agency's authority to achieve the lowest MFP for each selected drug.

We strongly oppose any arbitrary and unilateral requirement to destroy materials that conflict with best business practices and argue that such a policy is not material to CMS' authority to establish the lowest MFP.

Manufacturers need to maintain documentation for best price determination initial submission and refiles (up to three years), as this is important for internal controls and accounting purposes. In addition, the information may need to be retained for disclosure to the Department of Veterans Affairs (VA) as part of commercial sales practices disclosure. This arbitrary policy is especially concerning considering CMS does not clarify how it would approach situations in which determinations impact an active MFP. It is not a common or acceptable commercial practice to destroy material relevant to active contracts. When CMS makes a determination during an active IPAY, manufacturers will need to retain associated documentation of the active agreement.

D.1. Providing Access to the MFP (40.4)

Successful effectuation of the MFP within the Program is best supported via a data-driven, retrospective discount model facilitated by a third-party administrator (TPA)

Within the Program the manufacturer of a selected drug must provide access to the MFP to providers and pharmacies with respect to MFP-eligible Part B, MA, and Part D beneficiaries.²³ Manufacturers have no obligation to provide access to the MFP to providers and pharmacies on units dispensed to non-Part B, MA, or Part D beneficiaries (MFP-*ineligible* individuals). CMS proposes defining "providing access to

²² See, e.g., *Attia v. Google LLC*, 983 F.3d 420, 425 (9th Cir. 2020) (public disclosure of a trade secret generally "extinguishes[s] the information's trade secret status," resulting in loss of the associated property right); *Life Spine, Inc. v. Aegis Spine, Inc.*, 8 F.4th 531, 540 (7th Cir. 2021) ("Publication . . . destroys the trade secret").

²³ 1193(a)(3); see also id. 1191(c)(2)

the MFP” as ensuring that the amount paid by the dispensing entity (pharmacies, etc.) for the selected drug is no greater than the MFP. Duplicate discounts of the MFP and the 340B program are explicitly prohibited under the law, and the manufacturers are statutorily required to provide the *lower of* the MFP or the 340B price.²⁴

To achieve these goals CMS proposes that a manufacturer provide access to the MFP either by: (1) ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP or by (2) providing a retrospective reimbursement for the difference between the dispensing entity’s acquisition cost and the MFP. Under the retrospective model, manufacturers must ensure “reimbursement” within a fourteen-day period. J&J has significant concerns that CMS has proposed an entirely unworkable model given the parameters of the current pharmaceutical supply chain. Significant, meaningful changes are required for the Agency to achieve IRA implementation as required under statute. J&J ***strongly urges*** CMS to collaborate with the primary stakeholders within the pharmaceutical supply chain to advance a ***workable*** solution that is clarified in updated Guidance.

Successful Program implementation requires CMS to adopt and facilitate a ***data-driven retrospective discount model operationalized through a third-party administrator (TPA)***. A retrospective discount model best facilitates timely access to an accurate MFP for verified, eligible MFP beneficiaries. Doing so will significantly increase program compliance (and reduce program integrity risks), assure the Agency of a more successful path toward timely Program implementation and provide the best overall experience for Medicare beneficiaries and other stakeholders in the critical path to MFP effectuation. Further, a retrospective model eliminates the unintended impact to NFAMP calculations resulting from sales processed through wholesalers, thus reducing impact on other government pricing calculations.

The core attributes of our proposed data-driven retrospective discount model are:

(1) Aligned with statutory intent: CMS has the legal authority to permit and facilitate an MFP retrospective discount. The statute does not specify the process by which the manufacturer of a selected drug must provide access to the MFP, and CMS is granted broad discretion to establish procedures to implement the provisions of the Program.²⁵

(2) Offer a pathway for the MFP-eligible beneficiary to benefit from the MFP discount at the point of sale (POS), effectuated through the plans, not manufacturers: J&J is aligned that an MFP-eligible beneficiary will have timely access to MFP-based cost sharing at the POS. We are further aligned to CMS’ clarification that access to the MFP by Part D MFP-eligible beneficiaries at the POS will be effectuated through plans, not manufacturers. We emphasize that manufacturers are not party to the transaction among the Part D beneficiary, the pharmacy, and the plan or its PBM at the POS, and thus the logical interpretation of the statute is for CMS to establish and/or facilitate a pathway whereby the MFP is passed-through to the MFP-eligible Part D beneficiaries by those directly party to the transaction at the POS.

(3) Data-driven, providing manufacturers with access to critical claims data that enable verification of the MFP-eligible individual, prevent payment of both the MFP statutory discount and a 340B discount on the same unit and confirm the MFP discount amount: The same robust data-driven approach will also improve CMS’ auditing capabilities for compliance.

²⁴ 1193(d).

²⁵ IRA 1196(a)(3)

(4) Aligned to a low-burden, administratively straightforward, workable model for all stakeholders: A retrospective discount model is the least administratively burdensome, practical, and compliant approach to providing access to a validated MFP price for MPF-eligible beneficiaries. The retrospective approach will also provide predictability to the pharmacies who will not be administratively burdened with the establishment of numerous, different processes and requirements with separate manufacturers.

(5) Facilitate sound program stewardship: J&J strongly underscores the importance of a retrospective model to best position CMS to advance sound program stewardship. Specifically, a retrospective discount is the only valid approach to offering a mechanism through which critical parties to the negotiation can verify that the MFP-eligible unit, at the correct MFP price is dispensed to an MFP-eligible beneficiary. A core component of program stewardship is providing a meaningful mechanism by which the manufacturers can logically implement the prohibition on MFP-340B duplicate discounts across Part B, MA, and Part D. ***A retrospective discount model supports meaningful implementation on the prohibition of MFP-340B duplicate discounts as prohibited under statute.***²⁶ The Manufacturer is required to provide access to the MFP when the MFP is lower than the 340B ceiling price. When a 340B ceiling price is subsequently determined to be below the MFP, the manufacturer would be required to provide the covered entity the difference between the MFP and the 340B ceiling price.

Data verification is a critical path under any scenario and requires CMS to play *an active role* in facilitating manufacturers' access to data for verification. With respect to MFP-340B duplicate discounts, CMS has taken important steps toward advancing such a mechanism. For example, effective January 1, 2024, all 340B covered entities must use 340B claims modifiers when submitting Part B claims.²⁷ CMS has similarly proposed to require a 340B modifier or identifier on the PDE record for the purposes of excluding 340B units from the Part D inflation rebate calculation.²⁸ CMS must build upon these initial steps to implement the prohibition of the MFP-340B discounts and specifically require the use of a 340B modifier (or a non-340B modifier) and condition payment of the claim on accurate modifier use (as recommended below).

We urge CMS to directly respond to our request that fair and sound program stewardship principles are advanced within the Program. Particularly as the statute does not provide other safeguards and mechanisms to assure MFP units are appropriately furnished; there is no ability to audit dispensed MFP units, nor is there a dispute resolution mechanism that enables manufacturers to contest improperly furnished units, or other penalties imposed upon parties that engage in practices that fall outside of the provision of the law and Program.

A neutral third-party administrator (TPA) will advance program stewardship and minimize stakeholder burden. A retrospective discount operationalized through a TPA will align to all the principles outlined within this section. A TPA approach will leverage existing methods to offer the MFP-eligible beneficiary access to the verified MFP at the POS, significantly minimizes critical stakeholder administrative burden (pharmacists, plans, beneficiary, CMS, and manufacturers) and will advance the integrity of the Program. The approach adopted with the successful implementation of the Coverage Gap Discount Program

²⁶ 1193(d) (the manufacturer is required to only offer the lower of the MFP and the 340B price).

²⁷ CMS, Part B Inflation Rebate Guidance: Use of the 340B Modifiers (Dec. 20, 2022). Available at <https://www.cms.gov/files/document/part-b-inflation-rebate-guidance340b-modifierfinal.pdf>

²⁸ Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1860D-14B of Social Security Act, and Solicitation of Comments (Feb 9, 2023). Available at <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>

(CGDP), created by the passage of the Patient Protection and Affordable Care (Act) in March 2010 and implemented less than a year later in January 2011, is a helpful model for consideration that would also leverage CMS' existing resources to increase the likelihood of program success.²⁹

The critical role of the TPA is to allow the eligibility of the MFP claim to be verified and enable manufactures and health plans to match eligible claims with the correct retrospective discount amount. In doing so, the TPA will make required data fields available to manufacturers, and other parties as needed, on a detailed claims-level basis at the time of invoicing. In Appendix A we outline the Part D and Part B requested data fields required for the TPA to operate successfully. Most of these data fields are already made available through the PDE record which significantly reduces the burden on the TPA.

If CMS does not pursue a TPA, at a minimum CMS must outline the process by which manufacturers will receive access to the detailed claims data required to verify the retrospective MFP discount.

The fourteen-day requirement should be eliminated until CMS clarifies the payment parameters (including payment flow to intermediaries) and the ability of manufactures to verify MFP discount eligibility.

J&J is aligned with CMS establishing reimbursement parameters to ensure pharmacies and other dispensers are promptly paid and we underscore that such prompt payments are made possible with the facilitation of intermediate entities. However, a fourteen-day period is impossible given the current guidance. At a minimum, there is insufficient time for the manufacturer to confirm that a unit was furnished or dispensed to an MFP-eligible beneficiary using the accurate methodologies required under the statute (including the *lower-of* standard for MFP-340B). In more practical terms, it is impossible for manufacturers to exchange and confirm data to verify MFP eligibility and 340B non-duplicative claims within this period.

Further, once CMS has clarified the payment parameters and a data driven verification process, we also request CMS clarify that any imposed timeline (fourteen-days, or otherwise) will only apply to the transactional payment of the discount value owed to the dispenser and that the clock starts *only after* the manufacturer has validated eligibility for the rebate.

D.2. CMS should leverage existing metrics, such as WAC, within the retrospective discount methodology to define the MFP discount amount.

CMS' proposal to use actual acquisition costs (AAC) is unpractical and inappropriate in calculating the value of the MFP discount. First, AAC is only available at the individual prescription level, known only to the dispensing pharmacy. It would be a new requirement for pharmacies to report ACC, and unclear to whom in the supply chain pharmacies would have to report. Second, conflicts may arise in requiring a pharmacy to report AAC to the wholesaler, thereby offering the wholesaler access to new data that may influence their negotiation position with the pharmacists. WAC is a widely adopted price reporting metric and is the logical choice.

D.3. CMS must clarify its proposed ten-year record retention policy.

CMS plans to require a Primary Manufacturer to retain for at least ten years from the date of sale any records relating to sales of the selected drug. This proposal conflicts with the previously outlined record

²⁹ SSA 1860-D-14A, Public Law 111-148; Public Law 111-152

destruction policy, and we further underscore that a Primary Manufacturer *is not responsible* for any other manufacturer's records retention process.

E.1 Nonduplication with 340B Ceiling Price 40.4.1

Payment of a claim for reimbursement for a unit of a selected drug must be conditioned on the accurate reporting of either a 340B or a non-340B claims modifier, uniformly across all Medicare programs (Part B, MA, and Part D)

The statute prohibits MFP-340B discounts. To compliantly implement this provision, CMS must facilitate a mechanism that allows manufacturers the pathway by which to comply with the law. We appreciate the steps CMS has already taken to establish 340B claims modifiers within Medicare, but more must be done. Specifically, we are urging CMS to require the use and reporting of either a 340B modifier or a non-340B modifier (or both), and condition claims payment on the accurate use of the applicable claims modifier(s). Not only are these modifiers required for compliant implementation of the Program, but unfortunately there is a documented history of duplicate discounts permeating the 340B program, including widespread 340B covered entity non-compliance with respect to the analogous Medicaid-340B duplicate discount prohibition.³⁰ In addition, CMS should establish a comprehensive auditing program of 340B Covered Entities (CEs)' appropriate identification and reporting of units subject to 340B agreements. This process could be further facilitated by a clearinghouse which is responsible for identifying and verifying 340B dispensed units administered to Medicare enrollees.

F. Compliance with Administrative Actions and Monitoring of the Drug Price Negotiation Program (40.5)

J&J acknowledges that a manufacturer that enter into an Agreement with CMS must comply with monitoring compliance requirements. However, CMS does not provide guidance on actions or processes the Agency intends to undertake to advance these efforts. We urge CMS to provide manufacturers with these plans when available, and to provide advance notice and opportunity for manufacturers to respond to any monitoring or compliance requests. We ask CMS to allow for flexibility and feedback as it develops and rolls out these processes.

NEGOTIATION FACTORS (Section 50)

Section 1194 of the IRA requires a "consistent process and methodology" for MFP price-setting. Unfortunately, Sections 50 and 60 of the Guidance fall far short of meeting these statutorily defined standards. Critical components of the Program, namely the statutory factors and the price setting methodologies addressed within these sections of the Guidance lack substantial clarity and fail to provide stakeholders, particularly manufacturers, with the predictability and certainty needed to comply with the statute. The framework for the statutory factors lacks a beneficiary-focused vision, a clear pathway toward predictable decision making and severely lacks clarity on how the Agency will accept and use data to arrive at the MFP. Most concerning is the minimal discussion on how value will be determined, how this determination is aligned to Medicare beneficiaries' well-being, and how this will inform the selected drug's MFP. Instead, the initial guidance and Information Collection Request (ICR) places an inappropriate and overemphasis on the non-clinical, manufacturer-specific data that bear little to no influence on beneficiary health. Where CMS has advanced specifics on the factors' influence on

³⁰ See Government Accountability Office, Drug Discount Program: Federal Oversight of Compliance at 340B Contract Pharmacies Needs Improvement (2018), available at <https://www.gao.gov/assets/gao-18-480.pdf>. See also PSA 340B(a)(5)(A).

establishing the MFP, it does so with ill-conceived methods that exceed statutory authority and are damaging to biopharmaceutical progress, and to our beneficiaries.

Unfortunately, the lack of a “consistent process and methodology” continues throughout section 60 where CMS’ proposes unworkable approaches to establishing and effectuating an MFP within the Program.

We urge CMS to significantly increase their engagement with key stakeholders, extend the timelines for public comments and re-work a substantial portion of these sections to align with the statutory mandate of a predictable Program that employs consistent processes and methodologies in establishing the MFP.

Our factor-specific feedback follows in the section below; however, we strongly request CMS consider the following in a significantly revamped framework for the negotiation factors.

- Update the framework to align with our collective goals of promoting beneficiary health and well-being, improving quality of care, and appropriately considering the value of medicines. Regarding the approach and methods adopted by CMS in considering statutorily required factors, J&J strongly recommends that first, selected drugs should be primarily assessed on their impact to patient lives, health outcomes, and society. Manufacturer-specific data on non-clinical factors of selected drugs should be considered secondary to clinical effectiveness during the MFP price-setting process as they have less bearing on patient outcomes, and
- Advance clarity and predictability in how the statutorily defined factors will be used within the Program to determine the MFP; this explanation should be offered across all the factors and be transparent to all stakeholders, particularly those party to the Agreement. CMS should clearly delineate, in updated guidance, their approach to reviewing evidence and engage in a transparent, scientifically rigorous, consistent, replicable, and open process. Further, the CMS must clearly delineate how each of these factors will inform the MFP in a transparent process before the start of the negotiation process.

A. Manufacturer-Specific Data (50.1)

As outlined in Section 50.1 of the Guidance, CMS delineates and elaborates the data required for submission by the Primary Manufacturer. The Agency intends to require data on research and development (R&D) costs borne by the Primary Manufacturer and if these costs have been recouped, current unit costs of production and distribution, prior Federal financial support, data on pending and approved patent applications, and market data and revenue sales volume data. This section of the Guidance is supplemented by Appendix C, which provides additional definitions and description of data collected during the MFP price-setting process. While required by statute, we note that the factors included here bear little influence on Medicare beneficiary health outcomes and do not inherently reflect the value of the selected drug.

a. *Consideration of research and development (R&D) costs*

As described in Section 50.1 of the Guidance, CMS has indicated their intention to assess the research and development costs and the extent to which the Primary Manufacturer has recouped these costs. As outlined in Appendix C, these include costs incurred during pre-clinical research, for the submission of

post-Investigational NDA, FDA-required Phase IV clinical trials, post-marketing trials, abandoned and failed drug costs per molecule or moiety, and other R&D costs. As outlined in the guidance, these data are collected with the intention to determine if a Manufacturer has recouped these costs as defined by “global, total lifetime net revenue for the selected drug.”³¹

While collection of R&D data for the purposes of determining Primary Manufacturer cost recoupment is required by statute, the approach currently outlined by CMS is unnecessarily burdensome and the proposed calculation of R&D spending in the guidance may not be compatible with existing financial accounting practices. The approach also neglects the multi-faceted and interlinked elements that comprise the research ecosystem, which may result in an incomplete and inaccurate calculation of R&D investment. For instance, placing obligatory reporting requirements on the Primary Manufacturer to disclose certain costs could create confidentiality and antitrust challenges in collaborative efforts. Further, as the Guidance itself acknowledges, such data may not exist or be accessible, for instance in cases where a company has been acquired and no longer exists. We also caution CMS to ensure that interpretation of R&D costs avoid survivorship bias, which erroneously separates historic investment on one product from most other assets that have failed.³² While challenging to access and report at the individual drug level, it should be noted that all these investments are essential in supporting the maturation of medical innovation.

As such, we recommend that CMS simplify the R&D reporting requirements to allow the Primary Manufacturer to offer an attestation in instances where the manufacturer believes to have fully recouped the R&D costs. Under such an approach, CMS can satisfy statutory obligations and, when necessary, collect more detailed information in cases where the Manufacturer has not yet recouped costs and could influence the MFP price-setting process. Lastly, it is important to consider the unintended consequences of pricing approaches based on the cost of development and production (“cost-plus”) that have been found to be disincentivize R&D productivity and innovation and are not driven by product value.

When defining various components of R&D costs, we encourage CMS to consider inclusion of costs associated with monitoring the safety and efficacy/effectiveness of marketed, FDA-approved drugs. Experience has shown that the research conducted after a drug’s FDA-approval provides significant and meaningful evidence about the drug’s profile as it is used larger and more diverse populations than the clinical development program. While post-approval studies conducted may be FDA requirements or voluntary additional real world evidence generation and related scientific engagements include objectives focused on pharmacovigilance, health outcomes, and comparative benefit-risk to inform decision making across stakeholders (health authorities, HCPs, patients and payers). We encourage CMS to consider these efforts as material research expenses within this section of the guidance. It is essential in understanding the real-world safety and effectiveness of drugs, particularly in subpopulations and groups with specific unmet needs not represented in the clinical development program and aligns with the Agency’s intention to understand patient outcomes to implement value-based approaches to inform the MFP.

Lastly, CMS specified in Appendix C that manufacturers use a cost of capital rate of 8.1%. Ideally, this rate would be specific to each manufacturer, however, in the interest of operational simplicity, CMS could adopt a more standardized rate observed across industry. We are concerned as 8.1% is significantly lower

³¹ Guidance, Appendix C, ps. 83

³² Drakeman, D.L., Drakemaken, L. N., *From Breakthrough to Blockbuster, The Business of Biotechnology*. 2022.

than amounts suggested by current empirical data which provides a range from 10.35% to 10.57%.³³ The approach to arrive at these independent estimates is also consistent with established research cited in CMS' guidance.³⁴ We strongly recommend that CMS publish updated values to be consistent with current industry data.

b. Current Unit Cost of Production and Distribution

In consideration of current unit costs of production and distribution, CMS proposes to set costs as an average across Primary and Secondary Manufacturers for all direct and indirect costs associated with sourcing materials of the drug, delivery mechanism, packaging, shipping, and other operating costs. Under the current definition outlined in Appendix C, these costs are fixed and neglect the variability and market conditions that often determine production costs. Further, the definition of these costs excludes the relevant and appropriate programs that support patient access to medicines and physician education and runs counter to the policy objective of value-based and patient-centered care. We are also concerned that the definition of these costs uses a fixed-in-time determination which risks harming market dynamics and, under certain market conditions, could escalate drug shortages as noted by the FDA and recently experienced with certain essential medicines.³⁵ We encourage CMS to broaden its understanding of the costs manufacturers incur to bring medicines to patients to adjust for various market dynamics and to include spending on disease awareness, physician and patient education, and other programs that Medicare beneficiaries rely on for access to their treatments.

c. Prior Federal Financial Support

As proposed in the Guidance, CMS employs an overly broad definition of prior financial support for novel therapeutic discovery and development of a selected drug to set the MFP. Public-private collaboration and partnerships that gather and disseminate knowledge and mutually supportive multistakeholder efforts to advance scientific and medical discovery have brought, and will hopefully continue to, bring a great deal of value to patients and society.³⁶ We are concerned that the current approach may result in the perception that prior financial support could be used as factor for CMS to justify a reduction in the MFP. Not only is this an operationally complex task, but overly simplistic linkages to prior Federal financial support do not lend sufficient insight into the extensive work and contribution of Manufacturers in bringing the selected drug to market and may result in negative and unintended consequences. As such, we are particularly concerned about the inclusion of tax credits for orphan disease drugs as a form of prior Federal financial support, as adjustments to the MFP based on this could be antithetical to the incentives of drug development for the treatment of individuals, and Medicare beneficiaries, with rare disease. We strongly recommend removal of tax credits from the definition of prior federal financial support. We also urge CMS to limit this information solely to funding that resulted

³³ Values are based on average of 598 biotechnology and 281 pharmaceutical manufacturers, Damodaran, A. (2023). Cost of Capital and Equity. https://pages.stern.nyu.edu/~adamodar/New_Home_Page/datafile/wacc.html

³⁴ Prior published peer-reviewed economic literature cited by CMS also suggest using a rate of 11.5%. DiMasi JA, Hansen RW, Grabowski HG. The price of innovation: new estimates of drug development costs. J Health Econ. 2003 Mar;22(2):151-85. doi: 10.1016/S0167-6296(02)00126-1. PMID: 12606142.

³⁵ <https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions>

³⁶ Conti RM, David FS. Public research funding and pharmaceutical prices: do Americans pay twice for drugs? F1000Res. 2020 Jul 15; 9:707. doi: 10.12688/f1000research.24934.1. PMID: 33204410; PMCID: PMC7642989.

in a patent application containing a Government Interest Statement and/or research where a patent assignee was a US government agency.

d. Patents, Exclusivities, and Approvals

The proposal by CMS mandate disclosure of confidential patent information may hinder industry collaboration. For example, a Primary Manufacturer and Secondary Manufacturer may be collaborators advancing a particular drug with one mechanism of action to treat a particular disease in a certain therapeutic area. However, the Primary Manufacturer and Secondary Manufacturer may also be developing competing products with a different mechanism of action in the same disease and therapeutic area. In this scenario, if the collaboration drug is selected for negotiation, the Secondary Manufacturer could be forced to disclose confidential patent information to the Primary Manufacturer relating to their competitor product since the strategies for protecting both products may be scientifically intertwined (e.g., patent protection for assays, methods of treatment, combination therapies, etc.). Accordingly, this forced disclosure will disincentivize companies from collaborating, which will decrease the discovery and development of new innovations, which reduce patient choice and consequently harms patients. As such, we strongly encourage CMS to update its guidance to clarify that the submission of any non-public patent information by a Primary or Secondary Manufacturer should be discretionary. Taking that approach would, among other things, avoid significant questions that the Guidance would otherwise raise under the Fifth Amendment's Takings Clause.

As part of the negotiation process, Section 50.1 and Appendix C of the guidance require a Primary Manufacturer to submit to CMS non-public, and often highly confidential, patent application information. Section 50.1 (on page 35) provides that a Primary Manufacturer is required to report to CMS "[d]ata on pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the FD&C (Food, Drug, and Cosmetic) Act or section 351(a)". Further, Appendix C provides that, "[a] pending patent application is any provisional or nonprovisional patent application submitted to the United States Patent and Trademark Office for which a patent number(s) has not been issued." We are concerned that the broad and vague language used to describe indirect applications is too ambiguous and unclear. We echo PhRMA's comments on this matter and urge CMS to consider the applications that are directly related to the selected drug, as confirmed by Primary Manufacturer.

Additionally, CMS requires sharing data on pending and approved patent applications, exclusivities recognized by the FDA, and other applications as part of the negotiation process. However, the agency has not indicated how this information will be used to determine the MFP. It is important to note that a patent is a Constitutionally protected property right granted by the US Patent and Trademark Office that protects new and innovative inventions. Property rights are a necessary economic incentive that promote innovation, knowledge sharing, patient, and doctor choice, as well as economic growth. Moreover, patents provide an opportunity for pharmaceutical and biotechnology companies to recoup investments made to deliver new products and patient solutions, which is especially important since R&D investment is high risk and rife with failure. Similarly, marketing exclusivity is a key incentive for drug developers and awarded for different innovations that enhance patient outcomes. We recommend the guidance be amended to require that the MFP be at or near the relevant price ceiling for a drug protected by at least one existing unexpired patent or exclusivity.

e. Market Data and Revenue and Sales Volume Data

As outlined in Section 50.1 and Appendix C, Primary Manufacturers must submit to CMS market data and revenue and sales volume data for the selected drug to inform the negotiation process. As currently defined, these definitions are very broad and often considered confidential, proprietary information. In addition to PhRMA’s comments, we strongly urge CMS to guarantee that any information collected on this matter be discretionary. Further, we encourage CMS to provide the appropriate flexibility to allow either the Primary or Secondary Manufacturer responsibilities for disclosure and reporting of this information.

B.1.1. Non-FAMP Data (50.1.1)

CMS Should Align non-FAMP with the Veterans Health Care Act of 1992 (VHCA)

J&J urges CMS to adopt the existing annual non-FAMP which calculated based on the four quarters of a federal fiscal calendar year under the VHCA. Leveraging this existing calculation will minimize operational disruptions that may arise with the creation of a new price point based on the calendar year. While the statute mandates the submission of the non-FAMP for the “applicable year,” it does not specify that CMS use calendar year as opposed to a fiscal calendar year. We highlight this as an opportunity for CMS to leverage data already available and to align with the VHCA rather than creating a new calculated price point based on calendar year. All stakeholders would benefit from the resulting efficiencies.

J&J urges CMS to adopt use of the fiscal year instead of calendar year for reporting of non-FAMP data. CMS does not define a process for non-FAMP restatements or for addressing non-FAMP anomalies which is important for addressing scenarios in which restatements may be necessary or to account for anomalous non-FAMP data.³⁷ J&J encourages CMS to outline a process for non-FAMP restatements and anomalies in final guidance.

We ask CMS to clarify the submission requirements for drugs where there is no non-FAMP data in 2021. For this scenario, CMS states its intent to require the Primary Manufacturer to submit data on the non-FAMP, unit type and total unit volume for each NDC-11 of the selected drug for the first full year following market entry of such drug. However, no details are provided to define the phrase “market entry.” Therefore, we ask CMS to define market entry in its final guidance to provide more clarity around this requirement for manufacturers.

B.2. Evidence About Therapeutic Alternatives for Selected Drug (50.2)

a. Quality Adjusted Life Years (QALYs)

At J&J, we believe that a medicine’s value is most accurately measured by its impact on patients, caregivers, and society. Accordingly, we believe that any form of value assessment should reflect these aims by being holistic and include a treatment’s impact on not only the health system, but also society at large. We support CMS’s intention to consider the full range of effects of a treatment and be centered on the patient and beneficiary perspective. We agree with CMS that the QALY is highly flawed and discriminatory in measuring the value of human health, particularly for those beneficiaries that are

³⁷ See VA PBM “Dear Manufacturer” Letter (Oct. 13, 2022) under Compliance or Pricing Errors.

elderly, live with chronic illness, or disability and are aligned with the Agency’s decision to disallow use of QALYs in evidence submitted to inform the negotiation process.³⁸ The prohibition on Medicare reliance on QALYs as outlined in the SSA applies to the Negotiation Process and determination of the MFP and therefore QALYs should not be used in any context.

Beyond the discriminatory nature of the QALY, there are numerous other well-known conceptual and technical problems with estimating QALYs.^{39,40,41} While the techniques may be useful for hypothesis generation in academic settings, given their significant flaws, QALYs should be assessed against a higher standard in the context of informing CMS’ decisions that directly impact beneficiaries’ and their families’ access to healthcare. For example, “the EQ-5D, which is the most commonly used PRO [patient-reported outcome] within QALY calculations, does not meet the FDA’s standard for patient involvement and therefore does not have legitimacy.”⁴² As such, this measure is not fit for reflecting the values that patients have for different health states, disease conditions, and consequently the value of alternative treatments.

Further, the potential for discrimination with the QALY, and its adaptations, is not merely contingent upon the differences in expected longevity. Nuemann and Cohen state: “Moreover, there are concerns that cost-per-QALY ratios potentially discriminate on the basis of age *and* disability by favoring younger *and* healthier populations that have more potential QALYs to gain.”⁴³ (*italic emphasis added*) In the Guidance, CMS states that “*certain uses* of quality-adjusted life years (QALYs) will not be used in the negotiation process.” This language is ambiguous and could allow use of QALYs in certain therapeutic areas where patient benefit does not include “life extension.” We also remain concerned about the influence of QALY-based research, even if such data has been separated from submitted evidence. We strongly encourage CMS to provide updated Guidance that more clearly and definitively prohibit QALYs, and similar metrics in any and all evidence submitted to the Agency.

CMS also solicits comments from stakeholders on other metrics, in addition to QALYs that the agency should exclude from consideration during the negotiation process. We encourage CMS to avoid use of metrics adapted from the QALY, such as the Equal Value of Life Years Gained (evLYG). The evLYG is even more problematic than the QALY, as by definition, it *disregards* quality of life impacts during the period of life extension. As such, important patient-centered considerations such as the side-effects of treatments would be excluded from consideration. Researchers have noted that using the evLYG could harm cancer patients in particular.⁴⁴ Furthermore, the evLYG measure and the alternative HYT (health

³⁸National Council on Disability. *Quality-Adjusted Life Years and the Devaluation of Life with Disability*. November 2019. https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

³⁹Schlender M. Measures of efficiency in healthcare: QALMs about QALYs? *Z Evid Fortbild Qual Gesundhwes*. 2010; 104:214–26.

⁴⁰Beresniak A, Medina-Lara A, Auray JP, et al. Validation of the underlying assumptions of the quality-adjusted life-years outcome: results from the ECHOOUTCOME European Project. *Pharmacoeconomics*. 2015; 33:61–9.

⁴¹Gafni A, Birch S. Preferences for outcomes in economic evaluation: an economic approach to addressing economic problems. *Soc Sci Med*. 1995; 40:767–76

⁴²<https://www.ajmc.com/view/is-the-qaly-fit-for-purpose>—Browne J, Cryer D, Stevens W. Is the QALY Fit for Purpose? *Am J Accountable Care*. 2021;9(2):8-13

⁴³Neumann P, Cohen JT. QALYs in 2018—Advantages and Concerns. *JAMA*. 2018;319(24):2473-2474. <https://jamanetwork.com/journals/jama/article-abstract/2682917>

⁴⁴Cohen, J. T., Ollendorf, D. A., Neumann, P. J., *Will ICER’s Response to Attacks on QALY Quiet the Critics*. December 2018. <https://cevr.tuftsmedicalcenter.org/news/2018/will-icers-response-to-attacks-on-the-qaly-quiet-the-critics>

years total), have been shown to be logically inconsistent over time, which should negate their use by CMS.⁴⁵ We agree with the assessment of the National Council of Disability, an independent federal agency of the US government, that “(t)he QALY/evLYG system still relies on health utility weights to measure quality of life improvements, despite the fact that such measures are typically derived from survey data and do not account for the complexity of the preferences and experiences of people with disabilities.”^{46, 47} We thus strongly encourage the Agency to protect vulnerable beneficiaries and disregard studies using the evLYG or other generic measures. Aligned with FDA Guidance, CMS should prioritize disease-specific and patient-centric quality of life instruments that capture the value of therapies to the populations CMS seeks to protect.⁴⁸

b. Evaluation of Real-World Evidence and Process Guiding Review of Submitted Research

The Guidance outlines CMS’ proposal to accept and review information on selected drugs and therapeutic alternatives from the Primary Manufacturer, other manufacturers, and members of the public. Further, CMS intends to review existing literature and real-world evidence, conduct internal analytics, and consult subject matter and clinical experts to inform its decision making during the MFP price-setting process. While we are encouraged by the rigor CMS states it intends to use, the Guidance provides little information on the criteria, standards, and process that will guide its review. We encourage the Agency to provide additional clarity and ensure its process is transparent, replicable, and methodologically sound. We strongly encourage CMS to provide public transparency into the submission of all non-proprietary information on stakeholders’ reports on therapeutic alternatives that are considered. Further, to account for the interest of manufacturers’ fiduciary responsibility, CMS should provide additional clarity on the requirement of the submission on therapeutic alternatives and relevant data and allow manufacturers to make public any of their redacted information shared with CMS upon agreement to the MFP. Doing so allows for meaningful and productive engagement throughout the process and assurance that medicines are being appropriately assessed and guided by patient-centeredness.

We believe that manufacturers, patients, providers, and other members of the public should have clarity in the Agency’s rationale and approach in interpreting such a vast body of evidence across comparators and indications. Specifically, transparency into the criteria used and measures taken to ensure the highest quality of research are important determinants in maintaining the public’s trust with the Agency’s decision-making. We urge CMS to recognize the severity of different outcomes (e.g., symptomatic outcomes, hospitalization, mortality) when evaluating clinical evidence and to weigh endpoints

⁴⁵ Paulden M, Snowsill T, O’Mahony J, McCabe C. *Are the ‘Equal Value of Life Years Gained’ and ‘Health Years in Total’ Approaches Viable Alternatives to the QALY? Matters of Logic and Matters of Value.*

Event: Society for Medical Decision Making (SMDM) 42nd Annual North American Meeting

Video presentation: <https://www.youtube.com/watch?v=MtNKI2VfTJw>;

⁴⁶ National Council on Disability. *Quality-Adjusted Life Years and the Devaluation of Life with Disability.* November 2019. https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

⁴⁷ https://ncd.gov/sites/default/files/NCD_Alternatives_to_the_QALY_508.pdf National Council on Disability. *Policy Brief: Alternatives to QALY-Based Cost-Effectiveness Analysis for Determining the Value of Prescription Drugs and Other Health Interventions.* November 2022

⁴⁸ Food and Drug Administration. *Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Guidance for Industry.* December 2009. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims>

accordingly. After characterizing the clinical comparators and clinical value, CMS analysis should also allow for inclusion of both economic and societal value that matters to beneficiaries.

To guide this process, we recommend that CMS engage with the manufacturer regarding its thinking across the factors during the negotiation process, like a process used in other evaluations on evidence such as the Advisory Committee on Immunization Practices' (ACIP) Evidence to Recommendations framework. In addition, we recommend CMS hold public meetings and provide engagement opportunities with a variety of stakeholders, including patient advocates, to discuss the evidence and understand alternative therapeutic choice and patient preferences. CMS also states that it intends to review additional evidence independently and separately and conduct internal analytics. However, the Guidance does not provide any information describing the methodology it intends to utilize in examining additional research, and the experts and members of the public consulted during this process. As applied to both the evidence submitted to the Agency and its own internal research and analytics, we urge CMS to develop and publish more detailed standards for evidence considered in determining the selected drug's MFP.

c. Addressing Unmet Need & Evidence for Certain Subpopulations

We appreciate CMS explicitly stating its intention to avoid formulaic numerical price setting, highlighting a preference for the qualitative evaluation led by evidence on comparative clinical value over cost-factors in determining initial MFP. However, the agency should broaden the definition of unmet need beyond the availability of therapies to include the current drugs' therapeutic profile correlated to the needs of patients and subpopulations, especially those with historically disparate access or outcomes. CMS should take an approach that harmonizes the Guidance with orphan and pediatric regulatory exclusivities codified in other federal statutes.

In the Guidance, CMS notes that it will prioritize data and evidence that is specific to the Medicare population and favor evidence with products with existing evidence demonstrating impact to Medicare populations. In developing a drug and collecting data on the clinical impact of the product, manufacturers consider all populations that use the therapy. We appreciate the Agency's focus on safeguarding and promoting the health of Medicare beneficiaries and we seek to develop post-approval evidence that demonstrates the impact of therapies on specific populations, including Medicare beneficiaries. As the agency weighs the vast amount of data and research on a selected drug, we urge the Agency to consider the value of these therapies for a diversity of patients, particularly certain vulnerable groups. Aligned with the agency's focus on advancing health equity, we encourage CMS to also consider the value of studies with varied origins and primary objectives or populations.

NEGOTIATION PROCESS (Section 60)

A. Establishment of a Single Proposed MFP for Negotiation Purposes (60.1)

Simplified Application of the MFP Specific to Each Dosage Form and Strength (Sections 60.1, 60.2.1, 60.2.2, 60.2.3, 60.2.4, 60.5)

CMS proposes a complicated methodology to establish the MFP specific to each dosage form and strength. The statute provides CMS with the authority to apply a more simplified and appropriate approach to establishing the MFP specific to each dosage form and strength.

We agree that the statute requires CMS to negotiate the MFP for a selected drug and further directs CMS to establish procedures to compute and apply the MFP to each specific dosage form and strength, as

applicable. However, we disagree with the complicated methodology CMS proposes to (1) identify a single price for use at each step in the negotiation process and (2) to establish the price across all dosage forms and strengths. We are further concerned with the unintended negative impact this approach will have on beneficiaries. To aid the Agency, we propose an alternative, simplified methodology, aligned with the statute, which calculates the differentiated MFP applied to each dosage and strength. Our practical methodology is consistent with the statutory requirement and CMS’ intent “to publish the MFP at the per unit (e.g., tablet) level for each dosage form and strength associated with the selected drug.”⁴⁹

Our methodology will achieve five primary goals:

- Align with CMS’ commitment to maintain price variation “*specific to each dosage, form and strength of the selected drug*”⁵⁰,
- Alleviate the circumstance that the single MFP methodology generates a price above the statutorily defined ceiling price for a specific dosage form (see Table 1),
- Significantly reduce the administrative burden on the Program [by leveraging existing price reporting calculations and promoting transparency, reliability, and validity,]
- Establish equitable beneficiary cost-sharing based on beneficiary and provider-preferred dosage strengths and forms, and
- Mitigate disincentives for continued innovation and improvement of in dosage formulations, strengths, and indications.

For the Agency’s consideration, we outline below a workable, alternative methodology and urge CMS’ collaboration in response.

CMS’ Proposed Methodology Will Have Unintended Consequences for Beneficiaries

Impact on Cost Sharing for Beneficiaries

Calculating a single MFP across all dosage forms, regardless of whether an equivalency metric is applied, impacts the MFP-eligible beneficiaries co-payment for a selected drug. This approach will have an inequitable impact on copayments for beneficiaries who use different form, strength, or package sizes of the product. With CMS’ proposed approach, beneficiaries’ cost-sharing will be based on the Single NDA equivalent MFP, not the actual utilized product, resulting in cross subsidizing across different forms and strengths. This outcome is not intended under the Statute. Table 1 offers an illustrative example:

Table 1: Flawed Methodology and Impact on MFP-eligible Beneficiary Cost-Sharing with a Single NDA Equivalent MFP

⁴⁹ Guidance Section 60.5 ps. 58

⁵⁰ Guidance Section 60.2.4 ps. 46

NDC 9	Product Description	NDC 9 PDE Weighted MFP p/LUM	PDE W-Avg 30 Days Equiv Qty	NDC9 Weighted 30 Day Equiv MFP	Across NDC9 PDE Weight %	MFP Across NDC9 30 Day Equiv
		A5	A6	A7 (A5XA6)	A8	A9 (Sum A8*A7)
	<u>5MG Strength</u>					
12345-0125	BrandC 100 Pills					
12345-0125	BrandC 30 Pills	\$ 9.88	30	\$ 296.27	26%	
12345-0125	BrandC 90 Pills					
	<u>5MG Strength</u>					
12345-0234	1MLX 5MG					\$ 348.56
12345-0234	2MLX 5MG	\$ 367.36	1	\$ 367.36	74%	
12345-0234	3ML X 5MG					

100%

CMS' proposed approach would result in a single MFP of **\$348.56** rather than separate MFPs of \$296.27 and \$367.36 respectively at each specific dosage form NDC-9 level, and notably the single MFP across all dosage forms is higher for the beneficiaries on the pill form than the MFP ceiling specific to that dosage form. This is an unfortunate outcome, and not an intended consequence of the IRA.

Further, CMS' proposed approach encourages linear pricing over time, which fails to account for unique production costs of different forms, etc. Consider a 5MG tablet (per the above table): used very rarely, the manufacturer will produce a much lower volume, with a greater per unit production costs. Under the methodology proposed by CMS the higher per unit production cost will impact the co-pays of all strengths unless the manufacture prices the same price per unit for the larger 10mg (which may be used more frequently and have lower per unit production cost). It is an unintentional consequence that risks pitting beneficiary cost obligation against reasonable production-cost accounting. Not to be overlooked, another unintended consequence of the proposed approach would be to disincentivize volume-based discounts for differential package sizes utilized across differing sites of care.

Impact on Innovation to Better Address Beneficiary Need

We are further concerned with the broader unintended beneficiary consequences resulting from the reduced incentives for incremental innovation under CMS' proposed methodology. The development of new dosage forms and strengths reflect advances in clinical medicine and the demands of patients and clinicians to achieve improved medication management and tolerance, enhance adherence and reduce burden, among others. Ongoing product innovation of an approved therapeutic helps to improve response to patients' medical needs and preferences and serves to improve care and outcomes.

Recommended Approach is Aligned to CMS' Objectives and Significantly Streamlines the MFP Calculation

We are aligned with the Statute and the Agency that an MFP should be calculated specific to each dosage, form and strength (NDC-9) and account for the variation in prices *"specific to each dosage, form and*

strength of the selected drug”.⁵¹ Our recommended methodology, described below, calculates the ceiling price **for** the lowest unit of measure (LUM) of a selected drug and establishes **a metric** from which CMS may negotiate a **percent of the MFP ceiling** as described in Section 60.4 to arrive at the published MFP per LUM.

To calculate the MFP ceiling for the LUM, weighted to specific dosage forms (NDC-9), the following steps should be followed:

Step 1: Establish the MFP ceiling based on the calculations required by Section 1194(C)(1) using the LUM (Tables 2 and 3)

Specifically, section 1194(C)(1) sets forth the calculations for the MFP ceiling determination where the MFP ceiling is the lower of (i) the sum of the plan specific enrollment weighted amount (EWA) or (ii) an amount equal to the assigned applicable percent described in Section 1194(C)(3), of the average annual non-FAMP (aNFAMP). As Section 1194 does not prescribe how such calculations must be performed, a straightforward, simplified, and practical approach to calculate the MFP ceiling for the LUM level, weighted for the specific dosage forms (NDC-9) is most expedient, transparent, and reliable. Calculating the MFP ceiling at the LUM is consistent with existing claims billing methodologies and allows for straightforward comparisons within the calculation. Tables 2 and 3 illustrate this calculation. Tables 2 and 3 reflect an example of a product with two different dosage forms (i.e., pills and vials), each with a distinct NDC-9, and each NDC-9 with three different package sizes at the NDC-11 level. While we neither recommend, nor see the value in, providing the MFP ceiling in 30-day equivalents, the MFP ceiling calculated for the LUM can easily be converted to a 30-day supply by multiplying the MFP ceiling for the LUM to a price per 30-day equivalent supply quantity.

To determine the MFP Ceiling, perform two calculations: 1) the amount equal to the assigned applicable percent of the aNFAMP described Section 1194(C)(1)(C), as illustrated in the example in Table 2, below, and 2) the amount equal to the sum of the plan specific EWA as indicated in Section 1194(C)(1)(B), as illustrated in Table 3. Compare the results of each calculation and select the “lower of.” (See Table 4)

Establishing the MFP at the LUM for the specific dosage form will provide CMS with a metric that can be applied uniformly across dosage forms and strengths for purposes of MFP setting. (See Table 5).

To perform each calculation, there are three simple steps, described below:

1. Calculate the MFP Ceiling per package.
 - ^a Apply the 75% of the aNFAMP specific dosage form, see Table 2 Column A1⁵²
2. Convert the MFP Ceiling per package (NCD-11) to “the MFP Ceiling per unit” (LUM NDC-11).
 - a. MFP Ceiling per package divided by number of units within a package, see Table 2 Column A3
3. Calculate the weighted **MFP Ceiling per Unit** for each dosage form (NDC-9)
 - a. Sum of MFP Ceiling per Unit multiplied by NDC-9 PDE weight percentage, see Table 2 Column A5

⁵¹ Guidance section 60.2.3

⁵² assumes the assigned applicable percent from Section 1194(C)(1) is 75% for short monopoly drugs.

Table 2 MFP Ceiling Based on “Applicable Percent” of the Average NFAMP

NDC 9	Product Description	Assigned Applicable %	aNAMP* (Pkg)	Step1	Package Size	Step 2	NDC9 PDE %	Step 3
				NDC 11 NFAMP Ceiling MFP p/Pkg		NDC 11 MFP p/LUM		NDC 9 PDE Weighted MFP p/LUM
		S	N	A1 N*S	A2	A3 A1/A2	A4	A5 Sum A3*A4
	<u>5MG Strength</u>							
12345-0125	BrandC 100 Pills		\$ 1,035	\$ 776	100	\$ 7.76	1.1%	
12345-0125	BrandC 30 Pills	75%	\$ 396	\$ 297	30	\$ 9.90	87.4%	\$ 9.88
12345-0125	BrandC 90 Pills		\$ 1,188	\$ 891	90	\$ 9.90	11.5%	
	<u>5MG Strength</u>						100.0%	
12345-0234	1MLX 5MG		\$ 430	\$ 323	1	\$ 322.50	0.3%	
12345-0234	2MLX 5MG	75%	\$ 980	\$ 735	2	\$ 367.50	82.4%	\$ 367.36
12345-0234	3ML X 5MG		\$ 1,470	\$ 1,103	3	\$ 367.50	17.3%	
*Inflation adjusted aNFAMP (this could be replaced with "Enrollment weighted amount")							100%	

Table 3 follows the same steps as above but uses the sum of the plan specific EWA:

Table 3 MFP Ceiling Based on “Enrollment Weighted Average” (EWA)

NDC 9	Product Description	NDC 11 EWA p/Pkg	Package Size	NDC 11 MFP p/LUM	NDC9 PDE %	NDC 9 PDE Weighted MFP p/LUM
	<u>5MG Strength</u>					
12345-0125	BrandC 100 Pills	\$ 1,350	100	\$ 13.50	1.1%	
12345-0125	BrandC 30 Pills	\$ 405	30	\$ 13.50	87.4%	\$ 13.50
12345-0125	BrandC 90 Pills	\$ 1,215	90	\$ 13.50	11.5%	
	<u>5MG Strength</u>				100.0%	
12345-0234	1MLX 5MG	\$ 475	1	\$ 475.00	0.3%	
12345-0234	2MLX 5MG	\$ 950	2	\$ 475.00	82.4%	\$ 475.00
12345-0234	3ML X 5MG	\$ 1,425	3	\$ 475.00	17.3%	
						100%

Step 2: Select the “Lower of” the Applicable Percent aNFAMP or EWA to Determine the MFP Ceiling

Once each calculation is performed, compare the results of each of the two methods above, and select the lower of the two methods. See Table 4 below for an illustration of this comparison.

Table 4 MFP Ceiling Determination: Lower of “Applicable Percent” aNFAMP or “Enrollment Weighted Amount”

Table 2		Table 3		
NDC 9	aNFAMP Amount p/LUM	EWA p/LUM	Lower of	MFP Ceiling p/LUM
12345-0125	\$ 9.88	\$ 13.50		\$ 9.88
12345-0234	\$ 367.36	\$ 475.00		\$ 367.36

Step 3 Determination of the Proposed MFP for Negotiation Purposes Using the Ceiling as Basis

This metric establishes the ceiling price for the LUM. The example below illustrates how a percent of the ceiling can be applied specific to each dosage form and strength for negotiation purposes. This figure can be converted to a 30-day equivalent supply MFP. This approach also allows CMS to confirm the Proposed MFP for Negotiation Purposes does not exceed the Ceiling.

Percent Application of the MFP Ceiling Across Dosage Form and Strengths:

Apply a “percent application” to the MFP ceiling across all dosage forms at the LUM.⁵³

			Proposed MFP for Negotiation
NDC 9	MFP Ceiling p/LUM	% Application of the MFP Ceiling	MFP p/LUM
12345-0125	\$ 9.88	95%	\$ 9.38
12345-0234	\$ 367.36	95%	\$ 348.99

B.1. Determination of the Ceiling for the MFP (60.2.1)

We also urge CMS to provide manufacturers with the opportunity to review and reconcile the Agency’s collected data for purposes of calculating the ceiling for the MFP to ensure accuracy and completeness of the MFP ceiling calculation. This is important for transparency and enabling validation of calculations, but also important to a manufacturer’s ability to make counter offers during the negotiation process.

B.2. Sum of Plan Specific Enrollment Weighted Amounts (60.2.)

J&J opposes CMS’ proposed use of Direct and Indirect Remuneration (DIR) data to calculate for a selected drug an amount equal to the sum of the plan specific enrollment weighted amounts. Specifically, the statute states that the MFP ceiling must be determined by reference to the Part D negotiation price. The use of DIR data rather than PDE data conflicts with what is described in statute because, unlike the

⁵³ For illustrative purposes, assumes 95% for the CMS selected percent of ceiling price.

Part D negotiation price, DIR includes all price concessions including those received from manufacturers that are not passed through at the point of sale. The proposed approach does not align with statute or the existing Part D standard and should be modified accordingly.

B.3. Average Non-Federal Average Manufacturer Price (60.2.3)

While we agree with including steps to prorate to account for different prices for different strengths, forms, and formulations, we do not support CMS' intent to use WAC proration. Please see our comments for section 60.5 below for more details and for our recommended methodology and approach for determining the MFP Ceiling. Aligned with our comments under section 60.5, we also encourage CMS to consider separately each BLA/NDA for purposes of determining monopoly type.

B.4. Selection and Application of the Ceiling for the MFP (60.2.4)

Please refer to above comments

C.1. Developing a Starting Point for the Initial Offer (60.3.2)

CMS states that by using the net price of a therapeutic alternative as the starting point for the initial offer, the Agency is “able to focus the initial offer on clinical benefit by adjusting this starting point relative to whether the selected drug offers more, less, or similar clinical benefit compared to its clinical alternatives.” CMS then says that if the price of the therapeutic alternative is above the MFP ceiling or if there is no clinical alternative, then CMS will use the Federal Supply Schedule (FSS) or the “Big Four” price as the starting point.

J&J objects to the use of the FSS or “Big Four” prices in this manner. First, the use of these price points is inconsistent with the reasoning behind using the price of a therapeutic alternative—if the price of the alternative is above the ceiling or if there is no clinical alternative, the most consistent choice of a starting point is the ceiling price. This would most closely reflect the value of the therapeutic alternative and would be appropriate for any product with no clinical alternative since such a product clearly addresses an unmet need. In addition, the FSS and “Big Four” prices are inappropriate for use in the MFP price setting process because they are intended for specific non-Medicare populations within closed systems and do not represent a retail price. CMS should use the ceiling price as the starting point in proposing an initial offer when the therapeutic alternative's price is above the ceiling or if there is no therapeutic alternative.

CMS asks for comments on how to determine the starting point for the initial offer when there are multiple therapeutic alternatives. When considering multiple therapeutic alternatives, J&J recommends that it would be most appropriate to consider the highest-value therapeutic alternative. As CMS is setting up an untested system to determine prices which will have broad impacts on the incentives to develop new drugs and to seek additional indications, CMS should begin this process in a manner that minimizes harm to ongoing innovation by undervaluing selected drugs.

C.2. Adjusting the Starting Point Based on Clinical Benefit (60.3.3)

CMS says that it will evaluate clinical evidence, including data submitted by the public and the manufacturer, as well as a literature review, and will analyze Medicare data or “other pharmaceutical datasets” for utilization patterns, clinical data, or other information. CMS also states that the Agency may consult with clinical and academic experts.

J&J recommends that CMS consider the full range of benefits associated with the selected drugs. CMS should consider the impact of a selected drug on patients, caregivers and the broader society and give due weight to important considerations like convenience, added adherence, caregiver burden, and other societal impacts (e.g., impacts on incarceration or health system savings) in determining the initial offer. We also ask CMS to provide manufacturers the opportunity to recommend outside experts to weigh in on key issues, such as comparator selection and clinical/societal benefits.

In addition, J&J urges CMS to provide transparency and clearly explain to the manufacturer the data sources used and how CMS factored them into adjusting the initial proposed offer. CMS should include this level of detail in the initial offer and engage with the manufacturer prior to the initial offer to allow the manufacturer to make a meaningful counteroffer.

C.3. Analysis for Selected Drugs with Therapeutic Alternative(s) (60.3.3.1)

When evaluating alternative treatments for selected drugs, CMS states that it will consider whether a drug meets an unmet medical need if it treats a disease or condition “in cases where very limited or no other treatment options exist.” This definition of unmet need is unduly narrow and will not provide appropriate recognition of drugs that provide important clinical improvements as compared to alternative treatments.

J&J recommends that in determining whether a drug addresses an unmet need, CMS should consider the selected drug’s position in the current standard of care for the disease. If the selected drug is recognized as the most effective treatment for its indication based on being the standard of care, it de facto addresses a need that is unmet by existing alternatives based on its demonstrated effectiveness.

CMS also notes that it will consider the effects of the selected drug on specific populations. In addition to the groups specified in the guidance, CMS should consider impacts on subpopulations that have had historically disparate healthcare access and outcomes.

In CMS’ choosing a comparator as the alternative for a selected product that has multiple indications, generic comparators should not be used to deflate the MFP of the negotiated product when no other branded products are available to beneficiaries in one of the indications. Not only could choosing an older generation drug be an inappropriate therapeutic comparator, it also disincentivizes research in multiple indications and reduces treatment choices for diverse patient populations if being the only branded product in the indication would negatively impact the MFP.

C.4. Consideration of Manufacturer-Specific Data (60.3.4.)

CMS outlines its plans to adjust the preliminary price downward if R&D costs have been recouped and if the preliminary price is above the costs of production and distribution. J&J notes that this approach is inconsistent with the approach CMS describes to develop a value-based preliminary price. If CMS maintains that the preliminary price reflects the value of the drug vs. an appropriate comparator, then the suggested reductions would only serve to undervalue the selected drug. J&J recommends that CMS should consider these factors only as potential increases to the preliminary price to address R&D costs that have not been recouped or to avoid pricing below cost.

If the selected drug has patents and exclusivities that will last for several years, CMS states it may consider adjusting the preliminary price downward. J&J finds this reasoning perverse and is deeply problematic for two reasons. First, the existence of patents and exclusivities is evidence of value as

determined via the patent process or FDA review and therefore—the existence of patents or regulatory exclusivity should push the price UP, not down. Second, the IRA already includes a mechanism to address products that have extended periods on the market without generic or biosimilar competition (i.e., the ceiling-price step-down and related renegotiations) so CMS should not seek to penalize manufacturers again by reducing the initial offer due to the expectation of continued exclusivity. Further, the agency’s approach is arbitrary, capricious, and contrary to law, 5 U.S.C. § 706(2), because it would cause unnecessary conflict with the Patent Act and statutes that authorize regulatory exclusivities, and also because it would give rise to significant questions under the Fifth Amendment’s Takings Clause. Established principles of statutory interpretation—including the duty to construe statutes together as a harmonious whole and the constitutional avoidance canon—counsel in favor of taking an alternative approach that would not penalize manufacturers for obtaining and exercising patent rights.

D. Negotiation Process (60.4)

CMS intends to allow for a maximum of three in-person meetings after the manufacturer’s counteroffer has been rejected. J&J does not support or understand the justification to limit interaction with manufacturers in such a narrow manner.

This approach does not reflect a true spirit of negotiation or align with our experience. For example, negotiations with Pharmacy Benefits Managers (PBMs) and state agencies for formulary and Preferred Drug List (PDL) placement normally include a kick-off meeting and additional opportunities to meaningfully engage rather than adoption of predetermined limits on meetings. Given the importance of comparator selection in developing the initial offer, CMS should meet with the manufacturer upon drug selection to discuss selection of an appropriate comparator. In addition, J&J recommends that CMS should allow for a meeting with the manufacturer upon the manufacturer’s data submission to allow discussion of the clinical evidence package and to answer any questions prior to CMS’ development of the initial offer. CMS should also allow for a meeting prior to proposing the initial offer so that the manufacturer can provide input on the evidence sources CMS intends to use in finalizing the offer. These meetings should be in addition to the post-offer meetings that CMS discusses in the Guidance.

Given the centrality of the identification of therapeutic alternatives in the process CMS describes in the Guidance, CMS should inform the manufacturer about the selected alternative as soon as possible. Such notification will allow the manufacturer to prepare to review CMS’ initial offer and to respond with an appropriate counteroffer within the 30 days allowed in the guidance.

MANUFACTURER COMPLIANCE AND OVERSIGHT (Section 90)

A. Monitoring of Manufacturer Compliance (90.1)

CMS indicates it will closely monitor manufacturer compliance with terms of the agreement and aspects of the negotiation program, including tracking, monitoring progress, and engaging directly with manufacturers. CMS notes failure to comply with certain terms and deadlines could result in excise tax liability. As the negotiation process will include collection and disclosure of business sensitive and critical information, J&J emphasizes the need for sufficient time to evaluate all proposals for information and price before punitive actions such as CMPs or excise tax liability are asserted. Moreover, the possibility that failure to comply with the Guidance would result in imposition of tax liability further

underscores that the Guidance is a legislative rule that must be vetted through notice-and-comment rulemaking before taking effect.⁵⁴

B. Monitoring of Access to the MFP (90.2)

CMS outlines its plans for monitoring compliance with providing access to the MFP at the point of sale, including establishing a process for beneficiaries, dispensing entities, and other providers and suppliers to report violations to CMS. CMS notes it will investigate these reports and impose CMPs on Primary Manufacturers if CMS determines the Primary Manufacturer (or Secondary Manufacturer) failed to provide MFP. J&J is concerned that CMS does not outline any plans to institute a dispute resolution process or details on how it will engage with Primary Manufacturers following a report. Bedrock due process requirements dictate that CMS must, at a minimum, provide manufacturers with notice and an opportunity to be heard before the agency makes a finding of noncompliance or imposes penalties. The reporting process CMS outlines would be universally available to beneficiaries, dispensing entities and other providers and suppliers and therefore susceptible to incorrect information. It is important for program integrity that manufacturers be afforded the opportunity to engage in a dialogue with CMS in response to any report and a dispute resolution process if the Manufacturer disagrees with CMS' findings. Such a process should be broad and transparent, with advance guidance made available to manufacturers. We are aligned with PhRMA's comments on this topic.

PART D FORMULARY INCLUSION OF SELECTED DRUGS (Section 110)

CMS notes that "Medicare Part D plans shall include each covered Part D drug that is a selected drug on Part D formularies during Contract Year (CY) 2026 and all subsequent years for which the MFP of the selected drug is in effect during the price applicability period." While this statement is consistent with the IRA statute, we urge CMS to go beyond simply requiring selected drugs to be on formulary to safeguard appropriate drug coverage in Part D.

J&J is concerned that the price-setting process may lead plan sponsors to disadvantage access to selected or non-selected drugs via increased utilization management (UM) for any number of potential reasons, for example based on their preference for lower prices from the MFP or higher rebates from competing products. Without appropriate oversight, this is likely to lead to significant disruption for patients and providers, including high levels of non-medical switching and nonadherence.

This risk is likely to be exacerbated by the IRA's Part D redesign, which shifts substantial risk to plan sponsors. Plan sponsors may respond by narrowing formularies, increasing UM, and moving more products to higher cost-sharing tiers. These access barriers could seriously undermine the goal of the benefit redesign to make the Part D program more valuable for beneficiaries.

J&J recommends that CMS review and update its formulary review standards and update rules around plan coverage decisions, UM, narrowing formularies, medication exclusions, restrictive tiering, cost sharing levels and patient out-of-pocket exposure. CMS should conduct vigorous oversight of these activities and otherwise ensure that patients have meaningful access to selected drugs by limiting plans' ability to impose barriers to access those drugs.

⁵⁴ See, e.g., 5 U.S.C. § 553; Social Security Act § 1871; *Azar v. Allina Health Services*, 139 S. Ct. 1804 (2019).

APPLICATION OF MEDICARE PART B AND PART D PRESCRIPTION DRUG INFLATION REBATE PROGRAMS TO SELECTED DRUGS (SECTION 120)

Inflation rebates should only apply when the manufacturer has increased price.

CMS is soliciting comments as to whether additional guidance would be appropriate or necessary with respect to the interaction between the Program and the Part B inflation rebate program for years before IPAY 2028. We urge CMS to issue guidance to ensure the two discrete programs do not have an interactive effect. The benchmark CPIU and benchmark amount should have no bearing as to when a drug is selected, as this could result in unintended consequences including subjecting manufacturers to inflationary penalties when no price actions have been taken. When a drug is no longer a selected drug, the drug's benchmark price and the CPIU index resets to the most recent year measurements. If this happens, the manufacturer could be subject to the inflation penalty due to the CPIU index reset without taking any price action in the market post the "selected" designation – particularly when inflation returns to the normal rate of 1-2% annually. *See illustration below.*

■

Illustrative Example: No lag, Avg ASP= Quarterly. No list price actions or change in commercial contracting activities since upon drug selection. Biosimilar launched 2028, and drug no longer selected - resetting Benchmark CPIU and Payment period. ~Annual inflation of 3% (2023-2028)

	Channel Mix	2021	Applicable Year MFP		No Longer Selected*
			Y1 - 2026	Y2 - 2027	
		Net Price			1Q28
Medicare Part B	70%	60	\$ 50	\$ 51	57
Commercial	30%	60	\$ 60	\$ 60	60
Avg Calc ASP		60	\$ 53	\$ 54	58
Allowable Increase %			129%	133%	103%
Actual Increase			-	-	109%
Inflation Penalty %					6%
Selected Drug 2021-2027	33%				
Non Selected Drug 3Q26-3Q27	3%				

(Calculated ASP for applicable payment 1Q28)

In this hypothetical illustration, a drug is assumed to have a net price of \$60 and an average sales price (ASP) of \$60 in 2021. The drug is selected in 2026 with an MFP of \$50 and ASP of \$53. In 2027, the MFP is \$51, and ASP is \$54. In 2028, the drug is no longer selected because a biosimilar is marketed. After the drug is no longer selected in 2028, the price is no longer at MFP, and it is assumed that the Medicare Part B price is \$57 resulting in an ASP of \$58. During this time, the commercial price remains the same, no price increases have been taken, and annual inflation has been 3%. The benchmark CPIU resets, and any ASP increases over 103% will be subject to the inflation penalty. In this illustration, the actual increase in ASP since the applicable MFP year in 2026 is 109% resulting in a 6% inflation penalty. Based on this illustration, if a manufacturer does not want to be subject to an inflation penalty for a drug that is no longer selected and for which no price increases were taken, then the manufacturer

would need to keep the price at the MFP. Therefore, once a drug is selected, the manufacturer will always be constrained by the MFP even when it is no longer selected or else be subject to the inflation penalty.

CONCLUSION

J&J appreciates this opportunity to provide our extensive feedback to CMS on this Initial Guidance. Recognizing the significance of our comments, including our feedback in those sections in which CMS has not expressly solicited comment, we urge CMS to respond promptly and ramp-up the inclusion of manufacturers in the policy development process and to do so in a timely and transparent manner that will better serve current and future Medicare beneficiaries.

Sincerely,

A handwritten signature in black ink that reads "Jacqueline Roche".

Jacqueline Roche, DrPH
Head Payment and Delivery & Global Policy Institute
Johnson & Johnson Worldwide Government Affairs & Policy

Appendix: Part D and Part B Data Fields Required for the TPA

Data Item	PDE Field Name (if Applicable)
Date of Service (i.e., date filled) *	Date of Service
Prescription ID Number*	Prescription Service Reference Number
Part D Contract ID and Part D Plan Benefit Package ID	Plan Contract ID and Plan Benefit Package ID
De-identified Part D Beneficiary ID	Medicare Beneficiary Identifier
Prescriber National Provider Identifier (NPI)	Prescriber ID
Pharmacy NPI*	Service Provider ID
National Drug Code (NDC)*	Product Service ID
Days' Supply*	Days' Supply
Quantity Dispensed*	Quantity Dispensed
Fill Number*	Fill Number
Paid Date (date the Part D plan paid the pharmacy)	Paid Date
Claim Status (whether the claim was paid or reversed)	
340B and non-340B Indicators (if adopted by CMS)	
340B Clearinghouse Determination (if adopted by CMS)	
340B Ceiling Price (received from Clearinghouse)	
Maximum Fair Price (MFP)	
Pharmacy Actual Acquisition Cost (AAC)	
MFP Discount (AAC less the MFP)	
NDC Units (as submitted by provider/pharmacy/physician) *	
Encrypted Patient ID Code (Standard NCPDP)	

* These fields are already provided to manufacturers as part of the detailed data reports under the CGDP.



April 14, 2023

Dr. Meena Seshamani, M.D., Ph.D.
Deputy Administrator, Director of the Center for Medicare
Department of Health and Human Services
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Submitted electronically to IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Dr. Seshamani:

Kaiser Permanente appreciates the opportunity to comment on the *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments* (hereinafter “Initial Guidance”).¹

Kaiser Permanente is the largest private integrated health care delivery system in the U.S., delivering health care to 12.6 million members in eight states and the District of Columbia.² Kaiser Foundation Health Plan, Inc. and our health plan subsidiaries are Medicare Advantage Organizations (MAOs) and provide more than 1.8 million Medicare beneficiaries with prescription drug coverage through Medicare Advantage-Part D plans. Kaiser Permanente’s mission is to provide high-quality, affordable health care services and to improve the health of our members and the communities we serve.

Within our footprint, we maintain a primarily internalized pharmacy system, including over 550 outpatient, hospital, infusion, specialty and mail order pharmacy sites staffed by over 14,000 pharmacy personnel. Kaiser Permanente spends approximately \$10 billion annually on pharmaceuticals. Our Permanente Medical Group (PMG) physicians and other authorized practitioners prescribe, and our pharmacies dispense, over 90 million prescriptions annually.

We commend CMS’ efforts to provide timely implementation guidance on these key provisions of the Inflation Reduction Act (IRA). If implemented successfully, the Medicare Drug Price Negotiation Program (hereinafter the “Negotiation Program”) will be a critical mechanism to curb unsustainably high drug prices for Medicare beneficiaries. As a prescription drug purchaser that negotiates directly with pharmaceutical manufacturers to obtain the lowest possible drug prices for our members, Kaiser Permanente is well positioned to share recommendations on various aspects of the Initial Guidance to ensure CMS can effectively negotiate the lowest price for each selected

¹ 88 Fed. Reg. 16449 (March 17, 2023).

² Kaiser Permanente comprises Kaiser Foundation Health Plan, Inc., one of the nation’s largest not-for-profit health plans, and its health plan subsidiaries outside California and Hawaii; the not-for-profit Kaiser Foundation Hospitals, which operates 39 hospitals and over 700 other clinical facilities; and the Permanente Medical Groups, self-governed physician group practices that exclusively contract with Kaiser Foundation Health Plan and its health plan subsidiaries to meet the health needs of Kaiser Permanente’s members.

drug.

Section 30.1 – Identification of Qualifying Single Source Part D Drugs for Initial Price Applicability Year 2026

Although CMS is issuing the guidance in Section 30 as final without comment solicitation, we support how CMS intends to identify potential qualifying single source drugs for selection. Specifically, we agree that all dosage forms and strengths of a drug with the same active moiety or active ingredient and the same holder of a New Drug Application (NDA) or Biologics License Application (BLA) should be treated as one potential qualifying single source drug.

This interpretation is consistent with the statutory intent and will appropriately capture products offered by the same NDA/BLA holder that encompass several dosage forms and routes of administration of the same active moiety or active ingredient. Adopting a narrower interpretation would allow pharmaceutical manufacturers to shift more and more products outside the purview of the Negotiation Program based solely on modifications that do not materially differentiate the products.

Section 40.2.1 – Confidentiality of Proprietary Information

Manufacturers of a selected drug must submit certain information to CMS as part of the Negotiation Program. Within the Initial Guidance, CMS identifies which information will be treated as confidential and proprietary. This includes: (1) information on non-Federal average manufacturer price (“non-FAMP”); (2) research and development costs and recoupment; (3) unit costs of production and distribution; (4) pending patent applications; and (5) market data and revenue and sales volume data.

We support the confidentiality policy described in this section. Recognizing the proprietary and confidential nature of non-FAMP information, in particular, is critical to protect competition and the ability of purchasers to negotiate discounts. Publicly disclosing this information could lead to anticompetitive effects and higher drug prices for non-Medicare members, creating a chilling effect on manufacturers that might otherwise be willing to negotiate discounts.

Section 40.4 – Providing Access to the MFP

CMS intends to require that manufacturers provide access to the maximum fair price (MFP) by “ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP” or “providing retrospective reimbursement for the difference between the dispensing entity’s acquisition cost and the MFP.” Further, manufacturers must reimburse pharmacies, mail order services, intermediaries such as wholesalers, and other dispensers in a timely manner—within 14 days—the full amount of the difference between their acquisition cost for the selected drug and the MFP.

Although we support placing the responsibility on manufacturers to ensure the MFP is made available to MFP-eligible individuals and to pharmacies, mail order services, intermediaries and other dispensers, we urge CMS to provide flexibility for how manufacturers work with these entities to effectuate this requirement. For example, we do not recommend prescribing a specific mechanism, such as a chargeback or 340B-like process, to provide the retrospective reimbursement. For entities with limited or no participation in the 340B program, adopting such

processes would likely require significant technological infrastructure investments to incorporate new inventory and billing mechanisms. We are concerned with any prescriptive requirements that would entail such large systems changes. In many cases, purchasers may have existing rebate or other payment mechanisms that could be tailored to accommodate the new MFP requirements, and manufacturers should be able to work with their purchasers to find a solution that is least burdensome for both parties.

Section 50 – Negotiation Factors

Evidence About Therapeutic Alternatives for the Selected Drug

Kaiser Permanente strongly supports CMS' approach, as part of the negotiation process, to consider evidence about therapeutic alternatives to the selected drug as submitted by members of the public, including manufacturers, Medicare beneficiaries, academic experts, clinicians and other interested parties. We also support the use of nondiscriminatory health measures and versions of cost-effectiveness analysis to help CMS develop offers and review counteroffers under the Negotiation Program. CMS should be equipped with as much data and information as possible to inform their negotiations and drive toward the lowest price.

Evaluating data and evidence on therapeutic alternatives, including cost-effectiveness analysis, is integral to how Kaiser Permanente makes drug purchasing decisions and sets and manages our own formularies. We employ a rigorous, evidence-driven processes in close collaboration with Permanente Medical Group physicians and clinical pharmacists. On an ongoing basis, our pharmacists review and develop an objective, evidence-based analysis of a drug or therapeutic class. Our physician experts then review the evidence associated with each drug, including clinical trial data and the drug's efficacy among members within our system. Once we identify a preferred therapy based on such evidence, our pharmacy contracting team uses the data and information to inform their negotiations with the drug manufacturer. Once the processes of clinical evaluation and negotiations with drug manufacturers are complete, our clinician-led Pharmacy & Therapeutics (P&T) committees finalize the formulary and make updates as new information becomes available. Because prescribers within our system are not paid on a fee-for-service or pass-through basis, there is no incentive to structure our formularies in ways that result in higher use of expensive medications when less expensive medications have the same clinical efficacy. Prescribers trust our formularies because they are grounded in clinical evidence and developed through partnership with their peers. Based on this trust, clinicians tend to prescribe consistently with our formularies in the vast majority of cases.

It is important that evidence submitted to CMS about a drug's clinical benefit is strong, verified, and reliable. The quality and quantity of data submitted will vary by drug, such as by study design, population, and length of time since approval. It is our opinion that CMS will need proper parameters in place to curate the robust data collected on relevant drugs, for example, through a data collection framework, required template, or required executive summary. Data from entities other than from manufacturers should be identified and harnessed to inform drug value. To that end, we recommend considering a consortium to aggregate and verify data on drug outcomes from a variety of sources tracking this information. CMS can look to other countries for how they require manufacturers to submit data on comparative clinical evidence and pharmacoeconomic evaluation.

When considering evidence about alternative treatments to the selected drug, we recognize that

CMS may not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled or not terminally ill. Often, this includes studies which rely on quality-adjusted life-years (QALYs). Concerns and prohibitions on the use of QALYs have led researchers to develop alternative comparative effectiveness measures that do not differently value life extension based on the specified characteristics. These measures, which include the equal-value life year gained (evLYG) and others, are important metrics for CMS to consider when assessing the comparative effectiveness of the negotiation-eligible drug relative to therapeutic alternatives. Comparative effectiveness metrics and research are a critical tool to ensure drugs are priced fairly and serve as a check on manufacturers' long-standing practice of pricing drugs far above their value. We strongly urge CMS to affirmatively recognize that non-QALY metrics are appropriate, and indeed necessary, components of a meaningful negotiation process.

Manufacturer-Specific Data

As part of CMS' information collection process, we recognize that manufacturers will be submitting data on research and development (R&D) costs and the extent to which manufacturers have recouped those costs for selected drugs. While CMS is required to consider these data, we recommend placing greater weight on other data, primarily comparative effectiveness research that demonstrates clinical benefit and cost information on therapeutic alternatives. Given the lack of external, non-biased resources to help verify manufacturer R&D cost data, CMS should exercise caution in attributing significant weight to this information. As CMS evaluates ways to ensure the long-term success of the Negotiation Program, we recommend considering research and partnership with external stakeholders to gather unbiased data on manufacturer R&D costs that could help inform the negotiation process in future years.

Additionally, when considering manufacturer R&D cost information, CMS should be careful to ensure manufacturers are not overestimating such costs. For example, we are concerned about common scenarios where one manufacturer acquires another and may attribute R&D spending by the acquired manufacturer toward their total R&D costs, even when there are similar platforms or shared costs that do not warrant such inclusion. We are also skeptical in the instance where a manufacturer might claim their selected drug has not recouped its R&D costs. It seems highly unlikely that a manufacturer of a drug or biological product that has been on the market for seven or 11 years and is included among the 50 drugs with the highest total expenditures in Medicare has not recouped its costs.

Section 60.1 – Establishment of a Single Proposed MFP for Negotiation Purposes

For the purposes of determining a single price included in an initial offer, CMS intends to base the single price on the cost of the selected drug per 30-day equivalent supply (rather than per unit – such as tablet, capsule, injection – or per volume or weight-based metric), weighted across dosage forms and strengths, as applicable. CMS believes this approach aligns with the statutory requirement to negotiate an MFP across dosage forms and strengths and will also allow for a more direct comparison with therapeutic alternatives. CMS intends to translate the finalized MFP from an average price per 30-day equivalent supply back into per unit prices for the purposes of publishing per unit MFPs.

We support CMS in using a price per 30-day equivalent supply for the purpose of negotiating the MFP. In our view, a 30-day equivalent supply is a commonly understood metric that can be easily calculated and compared across drug therapies. This approach will simplify and enhance the negotiation process.

Section 60.3 – Methodology for Developing an Initial Offer

When determining an initial offer to manufacturers for a selected drug, CMS intends to: (1) identify therapeutic alternative(s), if any, for the selected drug; (2) use the Part D net price or the Part B average sales price (ASP) for the therapeutic alternative(s) to determine a starting point for developing an initial offer; (3) evaluate the clinical benefit of the selected drug, including whether the selected drug meets an unmet medical need and the selected drug's impact on specific populations (resulting in the "preliminary price"); and (4) further adjust the preliminary price by the enumerated negotiation factors. If there are multiple therapeutic alternatives, CMS intends to consider the range of net prices and/or ASPs as well as the utilization of each therapeutic alternative to determine the starting point.

When there are multiple therapeutic alternatives, we recommend that CMS choose the lowest net price and/or ASP among the range of prices as the starting point. When developing a starting price for an initial offer, CMS should also consider evaluating other relevant pricing metrics in addition to Part D net prices or Part B ASP such as prices paid by other public payers within the United States, as well as prices paid by other comparable countries. If the selected drug has no therapeutic alternative, if the price of the therapeutic alternatives identified is above the statutory ceiling for the MFP, or if there is a single therapeutic alternative with a price above the statutory ceiling, then CMS intends to determine the starting point for the initial offer based on the Federal Supply Schedule (FSS) or "Big Four Agency" price ("Big Four price"). If the FSS and Big Four prices are above the statutory ceiling, then CMS intends to use the statutory ceiling as the starting point for the initial offer.

While we agree that this approach is generally reasonable, we recommend that if the FSS and Big Four prices are above the statutory ceiling, CMS begin with a starting point that is a specified percentage below the statutory ceiling price (e.g., 20 percent lower than the statutory ceiling price). This specified percentage could be determined by examining other selected drugs in the Negotiation Program, for example as the average difference between the statutory ceiling price and the initial offer for other selected drugs with therapeutic alternatives. We believe that in no case should CMS begin with the statutory ceiling price as the starting point for the negotiation process as this leaves no room for a true negotiation.

Section 110 – Part D Formulary Inclusion of Selected Drugs

The Initial Guidance reiterates the statutory requirement that Medicare Part D plans shall include each selected drug on their formularies during Contract Year (CY) 2026 and all subsequent years for which the MFP of the selected drug is in effect during the price applicability period. Importantly, the IRA did not specify *how* selected drugs must be included on a Part D formulary. Therefore, Part D plans should continue to have flexibility in designing evidence-based formularies that support appropriate, safe and cost-effective access to covered drugs. This includes retaining the ability to remove a selected drug from the formulary when a therapeutically equivalent generic drug becomes available to the extent permitted under the IRA and Part D

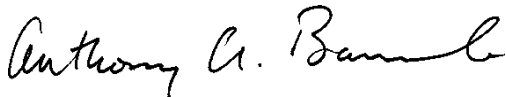
regulations. Also, when a generic drug or biosimilar becomes available, Part D plans should retain the existing flexibility to modify the brand name drugs' preferred or tiered cost-sharing status.

We strongly urge CMS to reiterate support for these flexibilities and refrain from applying any special formulary treatment toward selected drugs, such as establishing selected drugs as a protected class or requiring preferred placement within Part D formularies. We anticipate instances where Kaiser Permanente may have negotiated significant discounts on a therapeutic alternative to a selected drug, perhaps lower than the negotiated MFP, and requiring us to place the higher-priced selected drug in a preferred position on our formulary would lead to increased costs for members and jeopardize our ability to secure continued discounts on the alternative product. The Negotiation Program should not serve as a mechanism to reduce competition and create winners in certain drug classes.

* * *

We appreciate your consideration of our comments, and we look forward to working together to ensure the successful implementation of the IRA and the Negotiation Program. Please feel free to contact me at (510) 271-6835 or anthony.barrueta@kp.org or Simon Vismantas at (425) 677-1267 or simon.p.vismantas@kp.org with any questions or concerns.

Sincerely,



Anthony A. Barrueta
Senior Vice President
Government Relations

kalderos

Via email to IRAREbateandNegotiation@cms.hhs.gov

Dr. Meena Seshamani, M.D. Ph.D.,
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health & Human Services
7500 Security Boulevard
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program Guidance

Dear Deputy Administrator Seshamani:

Kalderos appreciates the opportunity to submit comments on the Centers for Medicare & Medicaid Services' ("CMS") Initial Memorandum on the Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026 (hereinafter, "Guidance").

Kalderos is building unifying technologies that bring transparency, trust, and equity to the entire healthcare community. We are on a mission to solve systemic problems of the healthcare system, redefining how the business of healthcare performs. Kalderos seeks to solve the problems in drug discount and rebate programs by connecting the stakeholders; enabling simple, streamlined communication; and applying machine learning to create smart data science tools. We are genuinely committed to being an honest broker administering a fair, balanced process assisting payers, providers, and manufacturers to ensure the right drug price is applied to the right transaction, in compliance with laws and contract terms.

I. Kalderos's Role in Discount and Rebate Compliance

Kalderos builds solutions to ensure that stakeholders comply with all statutory and regulatory requirements of discount and rebate programs, including those imposed by the Inflation Reduction Act of 2022 ("IRA") and other federal and state laws concerning drug pricing and reimbursement. To that end, Kalderos supports the goals outlined by CMS in the Guidance, particularly those goals related to program integrity.

The essence of Kalderos's honest-broker approach is to be fair to payers, providers, and manufacturers in a manner that is consistent with all applicable laws and regulations. To that end, Kalderos evaluated and developed solutions to facilitate coordination between dispensers and manufacturers, while simultaneously ensuring that there are systems in place to identify, dispute, and resolve noncompliance with drug discount and rebate programs.

However, despite years of attempts to educate providers and payers about how to prevent noncompliant discounts and rebates from happening, we continue to identify hundreds of millions of dollars each year in noncompliance. This fact leads us to conclude that traditional chargeback and rebate solutions are unlikely to be successful at preventing drug discount and rebate noncompliance. Accordingly, it is of vital importance that CMS' guidance regarding the Medicare Drug Price Negotiation Program ("Price Negotiation Program") adequately addresses the manner by which noncompliant Maximum Fair Price transactions can be prevented from occurring, and in

cases where noncompliance is unable to be prevented, provide a manner to identify and resolve disputes. Failure to do so would significantly weaken the purpose and intent of the Price Negotiation Program, as without effective safeguards against these issues, CMS will be unable to ensure that eligible individuals receive access to products at the Maximum Fair Price (“MFP”), without triggering a duplicate discount, consistent with the statute. Such failure could also open the Price Negotiation Program to challenge based on an arbitrary and capricious implementation of the Program.

It is with this background in mind that we offer the following comments:

- Guidance to Covered Entities Regarding Duplication of MFP Price & 340B Price: We are concerned that the Guidance does not make it clear that combining an MFP and a 340B discount on the same dispense is not permitted. Without CMS clearly stating that it is not permitted to obtain both an MFP and 340B discount on the same unit sold, covered entities and their contract pharmacies may not adequately adjust their systems and businesses processes to prevent the “stacking” of 340B and MFP prices on the same unit sold, which is clearly prohibited by the IRA statute.
- Mechanisms to Provide Access to the MFP Price: We appreciate CMS’ recognition that manufacturers must have the ability to offer the MFP through a retrospective rebate in order to ensure compliance with the statute. We agree that manufacturers should have the flexibility to determine how to provide access to the MFP and that such process should be reported to CMS to ensure transparency.
- Need for Claims Data: We are concerned that the Guidance does not provide effective mechanisms for identifying when a sale from a manufacturer is an MFP-eligible sale or preventing a single dispense from being subject to the MFP and a 340B discount. As a result, pharmacies, 340B covered entities, manufacturers, contract pharmacies, and other stakeholders will face significant confusion (and, potentially, time-consuming and expensive administrative burdens) when attempting to comply with the MFP provisions of the IRA in 2026. CMS should clarify that limited claims data must be submitted with a request for the MFP to ensure compliance.
- Auditing of Data Provided When Requesting MFP: While we appreciate CMS’ recognition that manufacturers should have the flexibility to implement MFP via chargeback or rebate mechanisms, we are concerned that unless manufacturers are permitted to include commercially reasonable and standard audit terms in agreements with dispensing entities relating to the mechanisms through which MFPs will be provided, there will exist a high risk of errors where dispensing entities may submit false or inaccurate information when requesting a MFP.
- Monitoring of Access to MFP: We are concerned that the process CMS relies on to ensure access to the MFP does not allow stakeholders to equally participate in program integrity measures. Specifically, we are concerned that CMS has not established a formal reporting process that would allow manufacturers to report

duplicate discounts, making it increasingly difficult for stakeholders to resolve duplicate discount issues.

I. Guidance to Covered Entities Regarding Duplication of MFP Price & 340B Price

We appreciate that the statutory language found in § 1193(d) of the IRA makes clear that the Primary Manufacturer of a selected drug is not required to provide access to the MFP for a selected drug to MFP-eligible individuals who are also eligible to receive the drug at the 340B discounted price if the 340B discounted price is lower than the MFP for such selected drug.

However, we are concerned that the Guidance does not expressly prohibit covered entities or their contract pharmacies from “accumulating” a transaction where a 340B-eligible beneficiary receives a product at MFP, potentially leading to a covered entity or contract pharmacy receiving both a MFP rebate and a 340B chargeback on the same unit sold. Instead, the Guidance places the burden on the manufacturer for preventing an MFP and 340B discount applying to the same dispense.

This is a particular issue in the context of the inventory management systems that many covered entities utilize, which are usually based on a replenishment model. Covered entities that utilize replenishment models, generally use accumulator software to tally the number of drugs dispensed to each type of patient (i.e, 340B-eligible patients and non-340B-eligible patients) and reorder the drug based on the utilization from each patient account. As HHS has previously recognized, replenishment models, and specifically the use of accumulator software, is an area ripe for duplicate discounts and other areas of noncompliance:

Some covered entities use software, referred to as accumulators, to track drug use for each patient type. The accumulator software would indicate which drugs are available to reorder on various accounts. In this example, the covered entity counts the units or amounts received by each 340B eligible patient. Once the covered entity has dispensed enough of a certain drug to equal an available package size, the covered entity could reorder that drug at the 340B price. **Once drugs are received in inventory, the drugs lose their identity as 340B drugs. . . . If the covered entity improperly accumulates or tallies 340B drug inventory, even if it is prior to placing an order, the covered entity has effectively sold or transferred drugs to a person who is not a patient, in violation of section 340B(a)(5)(B) of the PHSA. A similar violation would occur if the recorded number of 340B drugs does not match the actual number of 340B drugs in inventory, if the covered entity maintains a virtual or separate physical inventory.**¹

Additionally, we have experienced instances where covered entities have refused to work with manufacturers in good-faith when the manufacturer suspects that the covered entity may have

¹ HHS, 340B Drug Pricing Program Omnibus Guidance, 80 Fed. Reg. 52300, 52308 (proposed Aug. 28, 2015) (emphasis added).

caused the manufacturer to pay both a 340B price and a Medicaid rebate related to beneficiaries covered by a Managed Medicaid plan. These covered entities have stated that they believe the statutory language of the 340B program only prohibits covered entities from causing a duplicate discount related to FFS Medicaid programs, and as such, they refuse to engage in good-faith discussions related to Managed Medicaid rebates. As such, we believe that unless CMS expressly prohibits duplicating MFP and 340B prices on the same unit sold, some covered entities may not adequately adjust their pharmacy management systems and processes to prevent duplicating MFP and 340B prices.

Finally, we are concerned that service providers, including 340B third-party administrators, who offer what is referred to as “340B Recovery Services”² – services designed to re-examine transactions originally considered 340B-ineligible and reclassify certain transactions as 340B eligible – may not adjust their processes to ensure that prior transactions which received an MFP are not eligible to be re-qualified as 340B eligible without a clear and explicit prohibition set by CMS.

II. Mechanisms to Provide Access to the MFP Price

Section 40.4 of the Guidance addresses manufacturers’ obligation to provide access to selected drugs at the MFP to “pharmacies, mail order services, and other dispensers” with respect to MFP-eligible individuals, meaning, in practice, that manufacturers must ensure that “the amount paid by the dispensing entity for the selected drug is no greater than the MFP.”³ CMS requires manufacturers to provide access to the MFP by either “ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP” or “providing retrospective reimbursement for the difference between the dispensing entity’s acquisition cost and the MFP.”⁴ Further, manufacturers must submit their process for providing access to CMS.⁵

We appreciate CMS’ recognition that identifying when the MFP should apply at the point-of-sale, and ensuring that 340B pricing is not provided on the same dispense, will be a challenge. Manufacturers must have the ability to review claims data after a dispense, confirm the applicable price, and provide a retrospective rebate to the end customer. We further appreciate that manufacturers may take different approaches and agree that manufacturers should share their process with CMS to ensure transparency for all stakeholders.

Kalderos has developed rebate mechanisms to ensure program compliance in other government pricing programs. We are looking forward to using those experiences and learnings to help all stakeholders develop compliant systems to provide access to the MFP, consistent with the statute.

² See CloudMed, 340B Recovery, available at <https://www.cloudmed.com/government-navigation-suite/340b-recovery/> for an example of 340B Recovery Services.

³ See CMS, “Initial Memorandum on the Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026” at 31–32 (March 15, 2023).

⁴ *Id.* at 32. We further appreciate CMS’ confirmation that the use of “chargeback payments and rebate mechanisms among the pharmaceutical stakeholders in the private sector” are appropriate and that “the private sector may make modifications to these existing mechanisms to effectuate access to the MFP.” *Id.* at 65.

⁵ *Id.* at 32.

III. Need for Claims Data

CMS intends to leverage the use of plan identifiers to identify when the MFP applies. Namely, CMS states that the “use a unique Part D processor identification number (RxBIN) and Part D processor control number (RxPCN) combination” “will ensure that the pharmacy is able to identify at the point of sale whether the individual is an MFP-eligible individual.”⁶ The Guidance does not identify how 340B duplicates will be prevented and instead states “CMS intends to work with the Health Resources and Services Administration, which administers the 340B Drug Pricing Program, to help to ensure that the MFP is made available to 340B covered entities where appropriate.”⁷

Identifying when the right discount applies to the right sale, without triggering duplicate discount provisions, is a challenging task and costs significant time, money, and resources. Over the years, stakeholders have implemented several different approaches to prevent duplicate discounts, including modifiers, all of which have failed to be effective. Our experience with the use of modifiers finds them to be inadequate to consistently identify claims. For example, 340B covered entities must submit a code when seeking reimbursement from a state to identify when the entity dispensed a 340B drug. If a code were used on a claim, the state would exclude that claim when seeking rebates from the manufacturer. Despite the apparent benefits of using claims-level code data rather than dispensing entity claim data, modifiers have been largely ineffective in preventing duplicate discounts. For example, even if a 340B covered entity correctly identifies a claim as a 340B claim as opposed to a MFP claim, which does not occur consistently, that modifier may be removed at some point given the many touchpoints of a pharmacy, third-party administrator, or pharmacy benefit manager, among others. We understand that thirty-eight (38) states require claims modifiers from covered entities when submitting claims to Medicaid for reimbursement. For these states, Kalderos has identified approximately \$150,000,000 of 340B duplicate discounts over the last six years.

In light of these challenges, we urge CMS to not rely exclusively on modifiers and to encourage the sharing of claims level data to allow clear review of claims among stakeholders. In the context of the MDRP, stakeholders have repeatedly discussed the need for the transparent provision of robust claims data to improve dispute resolution processes. In fact, CMS itself has repeatedly emphasized the importance of claims data in disputes.⁸ CMS noted that providing claims level data may reduce the state’s administrative burden and expense of researching manufacturer dispute issues.⁹

Namely, rebate or chargeback requests for the MFP should include a minimum level of claims data. For example, claims covered by Part D should include, at minimum, the following data points: RxID; Date of Service; Pharmacy NPI or NCPDP ID; Prescriber NPI; NDC11;

⁶⁶ *Id.* at 65.

⁷ *Id.* at 66.

⁸ CMS, Best Practices for Avoiding 340B Duplicate Discounts in Medicaid (Jan. 8, 2020), available at <https://www.medicaid.gov/sites/default/files/Federal-Policy-Guidance/Downloads/cib010820.pdf> (stating ““when states provide claims level data to manufacturers, we would expect there to be a reduction in number of disputes due to more accurate information being provided” and that “manufacturers likely need claims level data for true invoice validation purposes.”).

⁹*Id.*

quantity dispensed; and actual acquisition price. Without manufacturers receiving claims data and using the claims data to validate and identify duplicate claims to CMS, accurately providing the MFP will be impossible.

IV. Auditing of Data Provided when Requesting MFP

Data inaccuracies related to the Medicare and Medicaid programs remain a significant challenge, with some estimating that such errors cost the Medicare and Medicaid programs up to \$100 billion dollars per year.¹⁰ CMS must permit drug manufacturers to audit the data submitted by dispensing entities when requesting an MFP rebate to reduce the risk of the submission of inaccurate data.

We note that it is standard commercial practice to permit drug manufacturers to audit the data provided by parties who request a rebate or chargeback. For example, contracts between manufacturers and wholesalers typically permit the manufacturer to audit supporting evidence relating to chargebacks. Similarly, rebate agreements between manufacturers and Pharmacy Benefit Managers (“PBMs”) typically permit the manufacturer to audit supporting evidence related to commercial rebates. These audits reduce the risk of inaccurate data being submitted by allowing the manufacturer the ability to verify the accuracy and legitimacy of discount or rebate requests.

In addition to the commercially standard practice allowing manufacturers to audit wholesalers and PBMs, similar audit language is typically included in contracts between wholesalers and pharmacies, as well as audit language found in contracts between PBMs and pharmacies. Should a manufacturer choose to contract with wholesalers or PBMs to effectuate MFPs between the manufacturer and beneficiaries/dispensing entities, the manufacturer’s standard audit language, combined with the audit language contained in wholesaler and PBM agreements with dispensing entities, will allow the manufacturer the ability to audit data submitted by dispensing entities.

We ask that CMS explicitly permit manufacturers and other shareholders, like Kalderos who are not wholesalers or PBMs, to enter into agreements with dispensing entities to audit the data submitted by dispensing entities requesting a MFP rebate.

V. CMS Must Provide an Adequate Process for Manufacturers to Report Issues in the MFP Process

The Guidance notes that CMS intends to establish a toll-free phone line and email by which “beneficiaries, dispensing entities, and other providers and suppliers” may report to CMS instances where an MFP was not made available.¹¹ Subsequent to reporting by these parties, CMS intends to investigate manufacturers and, if necessary, impose civil monetary penalties on manufacturers that have violated the MFP provisions. By contrast, while CMS “expect[s] manufacturers and other stakeholders”¹² to report instances of dispenser noncompliance, the Guidance does not provide any formalized reporting process that such parties may use, nor does it describe any action

¹⁰ See CNBC, “Inside the mind of criminals: How to brazenly steal \$100 billion from Medicare and Medicaid,” (Mar. 9, 2023) available at: <https://www.cnbc.com/2023/03/09/how-medicare-and-medicaid-fraud-became-a-100b-problem-for-the-us.html>.

¹¹ See Guidance, at pg. 66.

¹² *Id.*

kalderos

CMS will take to investigate claims against dispensers, nor does it describe what penalties, if any, will be imposed against dispensers found to be in noncompliance.

While we support CMS' intent to monitor the Price Negotiation Program, we are concerned that the Guidance does not provide manufacturers with an adequate opportunity to participate in program integrity. Specifically, we are concerned that the lack of a formalized process for manufacturers to report duplicate discounts or other MFP dispensing issues to CMS will limit manufacturers' ability to implement effective safeguards against such risks. Effective program integrity requires the participation of all parties with obligations under the IRA. We urge CMS to issue guidance establishing a process for manufacturers and other stakeholders to formally engage in the program integrity process.

* * *

Kalderos appreciates this opportunity to provide input about the Guidance. If you have any questions about these comments, please do not hesitate to contact me at 773-934-3672 or jdocken@kalderos.com.

Sincerely,

A handwritten signature in black ink, appearing to read "Jeremy G. Docken". The signature is fluid and cursive, with a large initial "J" and "D".

Jeremy G. Docken.



April 12, 2023

Via Electronic Delivery

The Honorable Chiquita Brooks-LaSure
Administrator, Centers for Medicare and Medicaid Services (CMS)
Department of Health and Human Services
Hubert H Humphrey Building, Room 445-G
200 Independence Ave. SW
Washington, DC 20201

IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Kinnate Biopharma Inc. appreciates the opportunity to submit comments on the Medicare drug price negotiation program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the CMS website on March 15, 2023.

Kinnate is a Nasdaq-listed US-based precision oncology company dedicated to developing new, targeted small molecule medicines for patients with advanced cancer, many of whom have been treated with multiple available therapies, but whose disease has progressed and have no other treatment options.

Traditional cancer therapies, such as chemotherapy, are a blunt instrument, often causing serious and sometimes irreversible side effects while treating the cancer. By contrast, targeted cancer medicines are a surgical scalpel, uniquely designed to target specific genetic drivers of cancer, and can spare the patient from most side effects. A more tolerated medicine means patients can be treated with higher doses, for longer durations, and have better outcomes and even functional cures.

Drug development is inherently risky, for small molecules and biologics alike

Small molecule medicines are a critical part of the inventory of therapies available to cancer physicians, and often complement and partner with biologics. Small molecules can access parts of the body which larger biologic molecules typically cannot (for example, passing through the blood-brain barrier to treat cancers that have spread to the brain). Many small molecule medicines can also be taken in pill form (orally), so patients can conveniently and privately treat themselves at home, without the costs and life disruptions associated with healthcare provider-administered medicines (biologics must be injected, typically infused over many hours at a treatment facility).

However, despite the fact that the costs and risks of developing small molecule drugs are the same as biologics, by reducing the amount of time drug developers have to recoup their investment prior to obligatory price negotiations, the Inflation Reduction Act of 2022 (the IRA) actively disincentivizes drug developers like Kinnate from investing in innovative new small molecules, and is likely to result in many fewer treatments for patients, not only in the next decade, but for all future generations.

We strongly support alignment of the timing for selection for pricing negotiations for small molecules to the 13-year provision for biologics, and encourage CMS to advocate for corresponding amendments to the IRA.

103 Montgomery Street, Suite 150
The Presidio of San Francisco
San Francisco, CA 94129

Website: www.kinnate.com 
LinkedIn: [Kinnate Biopharma Inc.](https://www.linkedin.com/company/kinnate-biopharma-inc) 



Subtypes of cancer are often very rare, and each subtype requires orphan incentives

Modern medicine has shown that cancer is not one disease, but hundreds of sub-diseases. For example, there are dozens of different subtypes of lung cancer, each with their own unique genetic drivers, and the most advanced and effective treatment utilizes a custom-designed medicine. Although lung cancer is not rare, many sub-types of lung cancer are very rare, affecting less than 5% of all patients with lung cancer.

A single drug has the potential to treat multiple rare subtypes of cancer, but per FDA regulations, each subtype requires its own development path and associated financial investment.

The IRA, as written, perversely disincentivizes drug developers from pursuing the full potential of medicines that could treat multiple, very rare diseases. The IRA's orphan drug exclusion applies only if there is one orphan designation per drug; a second designation would invalidate the exclusion, even if the designation is withdrawn or the drug is never developed for the second designated disease. As an example, a drug with a single orphan designation that could treat a US patient population of 180,000 would be exempted from price negotiation, whereas a drug with 4 orphan designations for populations of 10,000 patients each (40,000 patients total) would not be excluded and could be subjected to the IRA's price negotiation provisions.

Clearly this is nonsensical and contradictory to the intent of the Orphan Drug Act. This effect may be an unintended consequence of the IRA, as it actively discourages drug developers from pursuing important new therapies for US patients with rare conditions. We strongly believe revisions to the orphan exclusion provision are warranted as described in Annex 1 attached hereto, and encourage CMS to advocate for corresponding amendments to the IRA.

We are now in the age of precision oncology, and increasingly rare cancer subsets, so society needs more targeted therapies, not fewer. When patients are genetically matched with a targeted therapy and are spared the side effects of blunt instrument treatments, the clinical outcomes can be truly incredible. CMS's implementation of the IRA should promote the development of many more new treatments for rare diseases, not discourage it.

We appreciate your consideration of our comments as you develop the Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact the undersigned by telephone at (858) 299-4699 or by e-mail at mark@kinnate.com if you have any questions regarding our comments.

Yours sincerely,

A handwritten signature in black ink, appearing to be "Mj" or "Mark", written in a cursive style.

Mark Meltz
Chief Operating Officer and General Counsel

Annex 1

Section 30 Comments

Note: We recognize that CMS is not inviting comments to Section 30. However, we believe that comments to this section are warranted.

Provision	Harm Caused	Recommendation
(30.1) Medicare negotiation for small molecule and other NDA-path drugs at nine- years post-launch.	<p>Diversion of investment away from NDA-path drugs (small molecules, peptides, oligos, etc.) is likely to result in fewer therapeutic options for generations to come. For an overview of the harms of this provision see this open letter from Peter Kolchinsky (RA Capital) and Peter Thompson (Orbimed).</p> <p>Also, enclosed is a much more detailed yet plainly written explanation of how price setting at nine years post-launch dissuades investment.</p>	<p>Amend the IRA timing for NDA- path negotiations from 9- years to the same 13-year period as for BLA-path drugs.</p> <p>While 13 years is less than the typical 14 years of marketing exclusivity afforded by patent protection, investment can recalibrate slightly to one less year with very slightly higher launch prices so as to keep drug R&D a viable investment.</p>
(30.1.1) To be considered for the orphan drug exclusion, the drug or biological product must (1) be designated as a drug for only one rare disease or condition under section 526 of the FD&C Act and (2) be approved by the FDA only for one or more indications within such designated rare disease or condition.	<p>This provision perversely discourages companies from developing a single drug or biological product for than one orphan disease, especially where the patient population for secondary orphan indications are much smaller than the primary orphan indication, thus denying patients with very rare diseases the possibility of a life-changing treatment or cure.</p>	<p>The harms from IRA's treatment of orphan drugs could be mostly alleviated by amending the IRA to create small- and large- molecule parity for negotiation at 13 years (see above).</p> <p>CMS should broadly interpret the orphan drug exclusion to allow for multiple active orphan designations and multiple orphan approved indications for a single drug, provided that the cumulative prevalence of all orphan conditions remains within the orphan drug criteria.</p> <p>To help mitigate the harms to orphan drug development incentives, CMS should consider only active orphan drug designations for the</p>

		purposes of determining eligibility for the orphan drug exclusion (not including withdrawn orphan drug designations).
Other Comments		
(50.2) CMS' processes for determining the Maximum Fair Price for individual medicines as well as the relevance of "therapeutic alternatives" to the drugs it selects for negotiation.	Calculating cost-effectiveness, as embraced by ICER in the US and other HTA bodies elsewhere (e.g., NICE in the UK), is so simplified that it does not consider many demonstrable benefits of medicines (e.g., benefits to caregivers, reduction of risk for healthy people), resulting in extreme under-estimations of the value of new medicines. These calculations can then serve as rationale for plans to refuse coverage.	<p>CMS should acknowledge the value that a medicine brings to society before it decides how aggressively to lower its price (particularly in the case of NDA-path drugs that experience negotiation far sooner than they would experience generic competition). CMS should broadly account for a medicine's value elements, using a dynamic stacked cohort model that accounts for value to patients, to caregivers, and to the rest of the population whose risk is reduced by having the drug (i.e., if CMS is going to conduct a cost-effectiveness analysis (CEA), it should conduct a generalized CEA, not an over-simplified CEA).</p> <p>CMS should consider key product attributes like efficacy, safety, and ease-of-use in determining relevant "therapeutic alternatives" (the basis for CMS' opening bid).</p>
(40.2.2) CMS prohibitions on data disclosure and destruction of related documents.	The lack of transparency around the negotiation process makes it impossible for companies to understand which value components CMS is measuring in determining MFP, which in turn makes it more difficult to determine which documents will be needed by CMS and to develop projections regarding what a future MFP might be.	<p>CMS's process for determining value and cost- effectiveness should be transparent (vs. gag order and document destruction that is currently proposed). CMS should be able to publicly defend what it considers to be a "fair price."</p> <p>This can be achieved without disclosing company confidential information.</p>

April 14, 2023

Meena Seshamani, MD, PhD
Deputy Administrator
Centers for Medicare & Medicaid Services
Hubert H. Humphrey Building
200 Independence Avenue SW
Washington, DC 20201

Re: Comments on *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026*

Dear Dr. Seshamani:

Life Sciences Pennsylvania appreciates the opportunity to provide comments on the *Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026* (the “Guidance”). Life Sciences Pennsylvania is comprised of more than 880 members representing the entire life sciences industry – medical device companies, pharmaceutical companies, investment organizations, research institutions, and myriad service industries that support the life sciences in Pennsylvania. Pennsylvania is a global leader in researching and developing new therapies, devices and diagnostics that help patients live longer, healthier lives. This innovation is due in part to the policy and regulatory ecosystem we enjoy in the United States.

Life Sciences Pennsylvania supports policies in the Inflation Reduction Act (IRA) like the out-of-pocket cap for Medicare beneficiaries, that reduce costs for patients at the pharmacy counter. However, our membership has also expressed concerns that implementation could significantly inhibit investment in the research and development of new medicines as well as potentially impact patient access. At this time, we ask CMS for additional clarification in the guidance surrounding the following:

Preservation of incentives for innovation:

- Convene stakeholder panels to help inform key decision points (e.g., therapeutic alternatives, unmet needs, therapeutic advances, patient, and societal benefits) (Sections 50.2, 60.3)
- Establish Maximum Fair Prices (MFPs) for products addressing unmet needs or advancing patient care at the ceiling price (Section 60.3)
- Only consider manufacturer-specific data in instances where the selected product provides fewer benefits than therapeutic alternatives (Section 60.3)
- Clarify that products will be excluded from the MDPNP if they are approved for a sole orphan indication at time of selection, regardless of how many orphan designations the product may have (Section 60)

Ensure patient benefit and access:

- Establish standards that ensure patients will be no worse off in terms of access and cost-sharing, under the Negotiation Program than they were previously (Section 110)
- Provide meaningful opportunity for patient and stakeholder feedback, including on key decision points and on CMS's analyses (Sections 60.3, 40.2.2)

Thank you for considering these comments from Life Sciences Pennsylvania regarding preserving incentives for innovation as well as ensuring patient benefit and access. If you have any questions or concerns, please contact our Senior Director, Federal Policy and Public Affairs, Lara Flynn at lflynn@lifesciencespa.org.

Sincerely,

Christopher P. Molineaux
President & CEO

April 14, 2023

Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program Guidance

Dear Dr. Meena Seshamani,

We are writing to provide comments on the Initial Memorandum on Implementation of the Medicare Drug Price Negotiation Program published by the Centers for Medicare & Medicaid Services (CMS) on March 15, 2023. We are academic researchers with expertise in conducting pharmaceutical economics, outcomes, and/or policy research. Two of us are physicians and one is a pharmacist and health economist by training.

The Inflation Reduction Act mandates CMS to consider several factors in determining an initial price offer to the manufacturer of each selected drug. A key factor is “the extent to which such drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives.” In our comments below we identify and discuss specific complications that deserve careful consideration within the context of CMS’ proposed approach to handling this factor.

- (1) The appropriate selection of therapeutic alternatives is critical in determining the value and pricing of a drug. The initial guidance from CMS proposes to “begin by identifying therapeutic alternatives within the same drug class based on properties such as chemical class, therapeutic class, or mechanism of action before considering therapeutic alternatives in other drug classes.” Following this, the initial guidance proposes to determine CMS’s starting point for developing an initial offer via the average 30-day net price and/or average sales price (ASP) of the single therapeutic alternative (or the range of net prices and/or ASPs and utilization of each treatment in the case of multiple therapeutic alternatives).

While this proposed approach to selecting therapeutic alternatives seems reasonable, we are concerned about several downstream consequences. First, drugs from the same class with similar mechanisms of action often have similar clinical benefits, and they are often never compared in a randomized trial. From a practical perspective, high-quality evidence allowing for differentiating their relative benefits is often unavailable. Second, many drugs from the same class as the drug selected for negotiation may have been approved either contemporaneously or after the approval of the selected drug. In these cases, this means that the drug of interest does not actually represent a “therapeutic advance” over the therapeutic alternatives which are in the same therapeutic class. Finally, therapeutic alternatives within the same drug class are likely to have similar prices. Existing brand-name drugs have an anchoring effect on new drug launch prices in the same drug class in the United States. From a drug price negotiation perspective, CMS's proposed approach to selecting therapeutic alternatives from the same drug class may result in defaulting to setting prices based on the minimum discounts specified in the IRA in most cases (i.e., 25% for short monopoly drugs to 60% for long monopoly drugs).

Ideally, we believe that CMS should consider the entire universe of therapeutic alternatives, including older generation drugs, contemporaneous drugs, and recently approved next-generation therapies, without preference for starting with drugs of the same class. At a minimum, we recommend that CMS give priority to therapeutic alternatives with randomized trial evidence, particularly those that established the extent to which the selected drug represents a therapeutic advance for the disease. These should include the pivotal clinical trials that the U.S. Food and Drug Administration used for each drug approval.

- (2) Many of the drugs projected to be selected for negotiation have multiple indications, some even within the same disease. CMS appropriately plans to identify therapeutic alternatives for each indication. CMS should also consider various stages or lines of treatment within the same disease as multiple indications (e.g., first-line vs third-line treatment in cancer), identifying relevant therapeutic alternatives for each, and evaluating the extent to which the drug represents a therapeutic advance in each of those separate indications. CMS has also proposed to “adjust the initial offer based on the clinical benefit for an individual indication in cases where the clinical benefit of the selected drug is notably different than the therapeutic alternative for that specific indication.”

We recommend a modification to this approach when utilization volume varies substantially across its multiple indications. For instance, it is possible that a selected drug has large clinical benefit in relatively low-volume indications, and smaller benefits in high-volume indications. We suggest that CMS use Medicare claims data to identify the distribution of the selected drug’s volume across each indication. After developing a maximum fair price for each indication when compared with the relevant therapeutic alternative(s), an average price weighted by the frequency of that drug’s use in each indication can be calculated.

- (3) The selected drug and therapeutic alternatives may be administered over different durations than the selected drug (for example, treat to progression vs. fixed-duration cancer treatments). Hence, CMS’ proposed focus on comparing 30-day prices for the selected drug and its therapeutic alternatives is problematic and may misrepresent the “true” cost comparison between the selected drug and therapeutic alternatives. In addition to accounting for the length of treatment in calculating drug costs, we believe cost (beyond drug price) should be a part of assessing the extent to which a drug represents a therapeutic advance, including drug costs (incorporating duration of therapy), costs of managing side-effects, downstream treatments, and cost savings from avoiding side effects and/or other health complications.
- (4) The guidance document states that to adjust the starting point for the initial offer based on the therapeutic advance offered by the drug “CMS considered employing both a qualitative approach (e.g., adjusting the starting point upward or downward relative to the clinical benefit offered by the selected drug compared to its therapeutic alternatives) and a more thoroughly pre-specified quantitative approach. CMS intends to use a qualitative approach to preserve flexibility in negotiation, including the ability to consider nuanced differences between different drugs, for example interactions with other treatments commonly prescribed simultaneously for a condition or disease, and other factors that might not be captured in a more thoroughly pre-specified quantitative approach.”

We strongly recommend that even if CMS decides to use a qualitative approach to adjust the initial offer, it should still be informed using quantitative approaches that estimate value-based prices using decision-analytic methods in addition to qualitatively accounting for other nuances that may

not be captured in such quantitative approaches. Ideally, CMS should compute all dimensions of benefit and costs, strongly weighting the ones that patients value most. If impossible to account for all dimensions in the first year of negotiation, they should prioritize those that patients value most, for the disease(s) a drug is indicated for. Recently developed metrics, such as expected value of life years gained or health years in total, in conjunction with the Generalized Risk-Adjusted Cost-Effectiveness, can assess survival benefit and quality-of-life simultaneously without discriminating against the “elderly, disabled, or terminally ill.”

In summary, we recommend that CMS consider a broader range of therapeutic alternatives within and across indications for each selected drug and use established decision-analytic approaches to help account for multiple therapeutic alternatives and synthesize the multi-dimensional benefit and cost impacts of each comparison, integrating them into fair price recommendations.

Sincerely,



John Lin, MD, MSHP
Assistant Professor
UT MD Anderson Cancer Center



James I. Barnes, MD, MS
Acting Instructor
University of Washington



Jalpa A. Doshi, PhD
Professor of Medicine
University of Pennsylvania

April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20510

Submitted via IRAREbateandNegotiation@cms.hhs.gov

RE: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

The MAPRx Coalition (MAPRx) appreciates the opportunity to provide the Centers for Medicare & Medicaid Services (CMS) with comments regarding the implementation of the Medicare Drug Price Negotiation Program (MDPNP) for initial price applicability year (IPAY) 2026, published March 15, 2023.¹

Our group, MAPRx, is a national coalition of beneficiary, caregiver, and healthcare professional organizations committed to improving access to prescription medications and safeguarding the well-being of Medicare beneficiaries with chronic diseases and disabilities. The undersigned members of the MAPRx Coalition are pleased to provide CMS with our official commentary in response to your efforts to negotiate maximum fair prices (MFPs) for certain high-expenditure, single-source drugs and biological products.

MAPRx appreciates the opportunity to comment on how Medicare intends to negotiate with pharmaceutical manufacturers for lower prices on selected high-cost drugs. MAPRx believes it is critically important for beneficiaries to have access to innovative therapies and wants to ensure that MDPNP efforts do not exacerbate barriers to patient access.

MAPRx thanks CMS for seeking feedback on the negotiation process guidance, a step that was not explicitly required in the Inflation Reduction Act (IRA) statute. However, we remain concerned about the short 30-day comment period for the initial guidance, especially without knowing which products will be negotiated. The comment period provides little time to review the guidance and to consider and draft constructive feedback on the process by which CMS will negotiate drug prices for the first time in its history. Additionally, the inability of stakeholders to engage CMS while the agency is developing proposed regulations further limits the time permitted to provide input.

While we would have preferred an official Notice and Comment opportunity that would have facilitated an agency response directly to stakeholder feedback, we appreciate the opportunity

¹ Seshamani M. Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments. March 15, 2023. Accessed March 30, 2023. <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>

to share our concerns related to the MDPNP guidance. Overall as a coalition, we are focused on ensuring the following:

- Patient organizations have ample opportunity and ability to provide feedback on the negotiation process;
- CMS is transparent into how the agency factors external data into its final decisions (including the methodology deployed by the agency);
- The agency maintains access to a wide range of drugs within Part D and looks to minimize affordability challenges; and
- The agency establishes appropriate guardrails and ongoing oversight processes to continually evaluate the program for the purposes of refining when needed.

To that end, MAPRx is submitting comments on the following issues CMS addressed in the initial guidance:

- Highlighting the need for patient input to effectively maintain oversight and explore necessary program changes
- Maintaining beneficiary protections while implementing the new process
- Excluding orphan drugs from qualifying single-source drugs
- Excluding the utilization of Quality-Adjusted Life-Years in the negotiation process
- Offering feedback on future program guidance
- Reviewing the evidence about therapeutic alternatives for the selected drug
- Ensuring clear communication regarding the explanation for the MFP
- Exploring the future operation of the MDPNP
- Offering additional comments on the drug selection process

Patient Input Essential to Oversight and Continuous Improvement

As CMS initiates the implementation process, MAPRx requests the agency provide robust oversight to prevent unintended adverse patient impacts. Given the significant effect this new program and other changes, such as the redesign of the Part D benefit, will have on the drug delivery system, CMS must have proper systems in place to monitor impacts to ensure the program has the intended effect of increasing access and affordability for patients. At a minimum, CMS should monitor whether beneficiaries actually realize the expected savings, are not steered toward negotiated drugs inappropriately, do not face increased utilization management on either negotiated or non-negotiated drugs, and do not face other barriers to access.

In addition, it will be important for CMS to monitor the impact of negotiation on launch prices, inadvertent incentives for plans to prefer higher-priced drugs if they are able to achieve greater rebates (or inappropriate steering toward higher-priced drugs when Part B negotiation begins, due to higher provider fees), and disincentives to follow-on research on additional indications or new formulations that can demonstrate additional benefit such as greater adherence or reduced side effects.

Given that this guidance applies to the first year of negotiation, CMS will likely need to implement a mechanism for making needed adjustments. As such, we recommend CMS explore a formal process for seeking input from patients on the impacts of IRA implementation following the full implementation and on an ongoing basis.

MAPRx also requests guidance on how the patient community can best engage via the various information collection requests (ICRs). MAPRx appreciates the agency engaging with various stakeholder groups and is hopeful that the collaboration will continue with beneficiaries. To that end, we recommend CMS consider convening stakeholder panels or establishing other mechanisms to engage the beneficiary community and inform key decision points, including to obtain patient perspectives related to therapeutic alternatives and therapeutic advances, unmet need, considerations related to subpopulations and minorities, and patient experience and preference. MAPRx is committed to improving access to prescription medications and safeguarding the well-being of Medicare beneficiaries with chronic diseases and disabilities and welcomes the opportunity to provide CMS with patient-level data to ensure the best outcomes for patients.

Maintaining beneficiary protections while implementing the new process

MAPRx emphasizes the need for beneficiary protections and access to care while CMS is undergoing the new drug price negotiation process. We appreciate the Inflation Reduction Act's provision requiring all Part D plans to cover each drug with negotiated MFPs for all years for which the price is in effect during the price-applicability period. This provision helps ensure beneficiaries will benefit from the negotiation process and have access to the lowest-price drugs. MAPRx encourages CMS to monitor Part D plans to ensure beneficiaries have access to all negotiated drugs and provide opportunities to comment on beneficiary protections in the future. In addition, we urge CMS to provide strong monitoring and oversight of beneficiary access to both negotiated and non-negotiated drugs. For example, changes in formularies, tiering and cost sharing can impact a beneficiaries' ability to access prescription drugs under Part D.

Specifically, we seek clarification on CMS' interpretation of the requirement that negotiated drugs be covered by plans and if Part D plans will be allowed to apply utilization management (UM) tools or high cost sharing for the negotiated drugs. The initial guidance did not address UM techniques (e.g., step therapy, prior authorization, etc.) or cost-sharing requirements employed by Part D plans with respect to drugs with negotiated MFPs. While the patient community is incredibly supportive of the Part D redesign and out-of-pocket cap, we understand plans will face higher liability moving forward and therefore likely restrict coverage and/or access. Such UM techniques and cost-sharing requirements can create significant barriers and increase costs for patients by delaying the start or continuation of necessary treatment and negatively affecting patient health outcomes.^{2,3,4} Given this likely plan reaction to the higher liability, it is more important than ever that CMS create guardrails to ensure access to medicines by limiting burdensome barriers such as prior authorization and step therapy. By defining coverage requirements, CMS reduces the risk of plans denying coverage for products vital to a patient's comprehensive care plan. We also believe ensuring open access to negotiated drugs is simply the right thing to do. If a plan is receiving a lower price based on a maximum *fair* price, the benefit should be fully conveyed to beneficiaries through *fair* access. Conversely, it is crucial

² American Medical Association. Prior Authorization and Utilization Management Reform Principles. Accessed April 4, 2023. <https://www.ama-assn.org/system/files/principles-with-signatory-page-for-slsc.pdf>

³ O'Neil A, Calderbank S, Brown J, et al. Quantification of Utilization Management Barriers for Patients Initiating Therapy to Lower Lipid Levels. *JAMA Netw Open*. 2022;5(11):e2240513. Accessed April 4, 2023. doi:10.1001/jamanetworkopen.2022.40513

⁴ US Congress. House of Representatives. Utilization Management: Barriers to Care and Burdens on Small Medical Practices. 116th Cong, 1st sess. September 11, 2019. Accessed April 4, 2023. <https://www.govinfo.gov/app/details/CHRG-116hhrg37560/CHRG-116hhrg37560>

that CMS does not allow plans to prefer non-negotiated drugs by applying utilization management on negotiated drugs.

Excluding orphan drugs from qualifying single-source drugs

MAPRx appreciates the agency's openness for additional approaches on the orphan drug exemption. Our coalition is concerned the new law may hinder innovation, particularly for orphan drug indications. The Orphan Drug Act and other statutes, regulations and guidance create incentives to encourage the development of treatments for rare diseases. Rare diseases need incentives to encourage manufacturers to invest in developing treatments, however, MAPRx is concerned that the implementation of the IRA may undermine these incentives.

The law states CMS must exclude from price negotiations a drug for only one rare disease or condition and for which the only approved indication (or indications) is for such disease or condition. Unfortunately, if a manufacturer obtained an orphan designation to conduct research into treatment for another rare disease, the drug could be subject to price negotiation, even if it only has one approved indication. The law and its implementation thus remove the incentive for manufacturers to even conduct basic research and development into multiple rare diseases.

This disincentive has already been activated. Two manufacturers have stated they have cancelled further research of drugs, due to the disincentives built into the law and its implementation.⁵

MAPRx is concerned about the potential impact to investments in rare disease, and patients will suffer the most from such decisions.

Excluding the utilization of Quality-Adjusted Life-Years in the negotiation process

MAPRx is pleased that the Inflation Reduction Act (IRA) prohibits CMS from using the quality-adjusted life year (QALY) metric in the negotiation process. Any evidence that values extending the life of some individuals less than extending the life of other individuals based on disability status or age is completely inappropriate. All patients deserve to be treated equally, and thus we laud CMS' adherence to the statute and decision to separate out and exclude QALY metrics from evaluations of research that otherwise factor in QALYs. However, we are concerned that CMS may not effectively eliminate QALYs from analysis, or that CMS may over-exclude analyses that are otherwise helpful in establishing the value of a drug. Thus, we request that CMS offer more clarity into exactly how the agency will exclude QALY-based metrics from analysis of certain evidence. We also request that CMS highlight when and how the agency removes QALY-based metrics from consideration in MFP justification documentation. MAPRx is concerned that, unless CMS outlines a rigorous process for how the agency will consider evidence stemming from the use of QALY so as to not discriminate against individuals who are elderly, disabled, or terminally ill, such evidence could be inadvertently used that would be disadvantage said populations.

⁵ Endpoints News. Updated: Eli Lilly blames Biden's IRA for cancer drug discontinuation as the new pharma playbook takes shape. November 1, 2022. Accessed April 11, 2023. <https://endpts.com/eli-lilly-rolls-snake-eyes-as-it-axes-two-early-stage-drugs-including-a-40m-cancer-therapy-from-fosun/>

Fierce Pharma. As Amvuttra makes inroads in ATTR, Alnylam scraps heart disease trial interim analysis, rethinks another rare disorder plan. October 27, 2022. Accessed April 11, 2023 <https://www.fiercepharma.com/pharma/amvuttra-makes-inroads-attr-alnylam-scraps-heart-disease-trial-interim-analysis-rethinks>

While it is clear both in the statute and this guidance that QALYs will not be used as a base for evaluations, CMS requested input on what other measures might be appropriate or inappropriate. While we do not have a position on a specific measure, we do think that it is important that CMS rely on more than a single metric and explore a wide variety of sources by taking a holistic approach to this data. Patient value is multi-faceted, and any attempts to distill important dimensions of patient value and benefit into a single number is fraught.

Reviewing the evidence about therapeutic alternatives for the selected drug

MAPRx appreciates CMS considering different methods to evaluate the value of a prescription drug for patients. However, MAPRx cautions that this approach may not be appropriate for many drugs due to the difficulty in determining equivalence among drugs and biologics. Many times, it can be difficult to determine whether one pharmaceutical intervention is better than another for a patient. Throughout the coalition's existence (since 2005), we have consistently stated that the ultimate decision between available therapies should be left to the physician and the patient for this very reason. Patient experience needs to inform determinations of therapeutic equivalence. Additionally, while a selected drug may have therapeutic alternatives, the selected drug and any alternatives may not share the same specific indication or be used by the same population groups. Finally, some drugs may lack therapeutic alternatives as they are the only therapies in a given class to treat a specific condition. While MAPRx welcomes robust competition and options for patients, we support patient access to these critical therapies.

MAPRx is concerned about the unintended consequence that this specific provision may have on future access. Choosing lower-cost, therapeutic alternatives to drive down the price of the selected drug could disincentivize manufacturers from investing in therapies to treat specific indications or specific populations. With the potential to be linked to a lower-cost product with a questionable efficacy in a narrower population, manufacturers may opt against focusing on innovations for certain population groups or exploring additional indications to determine if their products have further benefits.

Offering feedback on future program guidance

We appreciate the opportunity to comment on initial program guidance for IPAY 2026 and seek clarification on processes for soliciting feedback moving forward. We request visibility into the opportunities to provide input into adjusting future program guidance and if there will be a comment opportunity to inform negotiation for IPAY 2027 and beyond. We believe that CMS may need to reevaluate its methodology for various pieces of the negotiation process, including aggregating drugs to determine MFP. As this is a new program implemented in a non-traditional manner, we believe CMS should be nimble and responsive to feedback from stakeholders as the policy is implemented year over year. To that end, CMS should establish a meaningful process for 1) patients and other stakeholders to provide consistent feedback on the experience of IPAY 2026, and 2) CMS to evaluate policy decisions made for the initial year of negotiation and incorporate necessary changes quickly for future years.

Ensuring clear communication regarding the explanation for the MFP

The explanation for the MFP will be a critical tool in the continuous improvement of the negotiation program, as well as a tool for the patient advocacy community to learn and improve our ability to participate in the process. We urge CMS to assure that these explanations are clear, accessible, and transparent. We also ask that CMS include critical information about what data was used to develop the MFP and how specifically it was used. We are especially

interested in information about how patient experience data was incorporated. Including this information in the explanation will help patient advocates develop the most useful data for future negotiations.

Exploring the future operation of the MDPNP

MAPRx respectfully requests further information on how the 2026 negotiation process will inform Part B negotiations in future years. Such information will enable stakeholders to have greater clarity into the future operations of the MDPNP and to plan accordingly.

Offering additional comments on the drug selection process

Although we are aware that you are issuing Section 30 on drug selection as final, we have a few comments we hope CMS will consider as the agency implements the drug-selection process for negotiation.

For example, we are concerned about the effects that the aggregation of drugs with the same active moiety or active ingredient in the selection process could have on subsequent research. We worry that aggregation could disincentivize research into additional indications or potential reformulations that improve patient adherence and/or outcomes. Without appropriate guardrails such as more nuanced definition, this initial guidance may discourage these types of improvements. While we understand the desire to eliminate potential gaming of extending patent life or time before negotiation, we fear this may be an overly broad approach that does not consider the patient perspective on whether reformulations demonstrate an improvement to patient care and feel there are better approaches to address this issue. We caution the agency against advancing this approach without appropriately assessing the impact it may have on incremental treatment improvements that can greatly benefit patients. If CMS is unable to reconsider this approach, we request that you undertake future notice and comment processes with adequate time for stakeholders to consider the impact of selection criteria as the negotiation process is implemented.

Conclusion

We strongly uphold that decisions on value are best taken when patient organizations can engage in the process and when patients are not limited by coverage policies that restrict access to products that best meet their individual needs. Thus, we urge CMS to carefully consider these comments for this and future guidance and allow for patient voices to be heard and emphasized throughout the negotiation process.

Thank you for your consideration of comments on the initial guidance of the implementation of the MDPNP for calendar 2026. The undersigned members of MAPRx appreciate your leadership to improve beneficiaries' access to products in Medicare Part D. For questions related to MAPRx or the above comments, please contact Bonnie Hogue Duffy, Convener, MAPRx Coalition, at (202) 540-1070 or bduffy@nvgllc.com.

Allergy & Asthma Network
Alliance for Aging Research
Alliance for Patient Access
ALS Association
American Association on Health and Disability
American Kidney Fund

Association of Hidradenitis Suppurativa and Inflammatory Diseases
Color of Crohn's and Chronic Illness
COPD Foundation
Derma Care Access Network
Epilepsy Foundation
GO2 for Lung Cancer
HealthyWomen
Lakeshore Foundation
LUNgevity Foundation
Lupus and Allied Diseases Association, Inc.
Lupus Foundation of America
Muscular Dystrophy Association
National Kidney Foundation
National Psoriasis Foundation
Partnership to Advance Cardiovascular Health
RetireSafe
The AIDS Institute
The Headache & Migraine Policy Forum

April 13, 2023

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Submitted via email to: IRAREbateandNegotiation@cms.hhs.gov

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Centers for Medicare & Medicaid Services
U.S. Department of Health & Human Services
P.O. Box 8013
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RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear. Dr. Seshamani:

The Massachusetts Biotechnology Council (MassBio) appreciates this opportunity to submit comments on the initial guidance regarding implementation of the Medicare Drug Price Negotiation Program (the “Negotiation Program”) established by section 11001 and 11002 of the Inflation Reduction Act (IRA) (the “Guidance”).

MassBio represents the premier global life sciences and healthcare hub of Massachusetts, which has a vibrant biomedical research and development community that is a global leader for medical discovery and innovation. MassBio’s 1,600+ member organizations are dedicated to preventing, treating, and curing diseases through transformative science and technology that brings value and hope to patients. MassBio’s mission is to advance Massachusetts’ leadership in the life sciences to grow the industry, add value to the healthcare system, and improve patient lives.

MassBio is deeply concerned about the impact the Negotiation Program will have on the future development of innovative and life-saving therapies, as well as on the world-leading small and emerging biotech companies based in Massachusetts. Through both a member survey and the collection of anecdotal evidence, MassBio has already identified concerning signals with respect to the IRA’s impact on innovation in Massachusetts. Based on these early signals, we believe the program’s framework will likely lead to less investment in biotech companies that work on the most difficult and risky science, and thus ensure significantly fewer resources are dedicated to the development of rare disease drugs and the hardest to treat diseases such as Alzheimer’s disease, cancer, and diabetes.

Given the potential impact on innovation and thus on vulnerable patient access to life-saving therapies, we urge CMS to adopt a “do no harm” approach in implementing this program that errs on the side of mitigating against the potential disincentives created by the program’s framework, and that allows the agency to make corrections as needed to preserve innovation.

We also urge CMS to carefully examine the impact of the law in Massachusetts. In light of Massachusetts’ unique role as the hub of companies directly engaged in research, development, and manufacturing of innovative products that improve the lives of people in the United States, Massachusetts

will be a “canary in the coal mine” in terms of changes to the system, and will thus be a good test case to see how IRA implementation affects the biotech industry. MassBio also plans to continue to survey our membership and perform other data-driven approaches to monitor the impact of the law, and we look forward to serving as a resource for CMS as the agency begins to track the impact of the IRA, particularly in Massachusetts.

Below we provide an overview of the innovation ecosystem in Massachusetts, as well as our comments on specific aspects of the Guidance, which are informed by the initial survey of our diverse and extensive membership. We would also appreciate the opportunity to meet with CMS to further develop and explain these ideas.

I. Background: The Innovation Ecosystem in Massachusetts

The innovation ecosystem is crucial to bringing a biopharmaceutical product to market and is composed of three, interrelated parties that interact in collaborative processes to move products from bench to bedside. These parties include: (1) small biotech companies and academia; (2) venture capital firms; and (3) larger pharmaceutical companies. Each of these parties serves a unique and vital role:

- Small biotech companies and the academic research community often partner to gather the necessary talent, engage in research, and pursue the latest scientific discoveries with the potential to develop viable treatments for a wide range of diseases and medical conditions.
- Venture capital firms provide equity investments in new and emerging biotech companies, to allow these companies to have the necessary capital and resources to advance through the different stages of the drug research and development process, particularly from proof of concept to actual clinical development.
- Large pharmaceutical companies help with the costly and burdensome process of bringing a new drug to market by contributing expertise and additional resources to the drug development pipeline, particularly through the use of diverse arrangements with emerging biotech companies, including acquisitions, licensing, and co-promotion.

All of these parties are essential components of the drug development and commercialization process. However, as the recent collapse of the Silicon Valley Bank has shown, this ecosystem is fragile and can be significantly disrupted if just one of the parties suffers a setback. For instance, while not a direct target of the law, venture capital investment choices do not operate in a vacuum, and are significantly impacted by long-term market dynamics, the ability to obtain a return on investment, and the inherent opportunity cost of specific investment decisions.

As noted above, in early 2023, MassBio surveyed its membership regarding the IRA’s immediate impacts, as well as member perspectives regarding certain regulatory and legislative policies that could mitigate those impacts.¹ A diverse cross-section of members responded to this survey, with a third of respondents having 10 employees or less. The majority of respondents indicated that they have already reconsidered their business strategy as a result of the IRA, and the vast majority also indicated that they have seen a shift in how investors are generally approaching biotech investments. This is consistent with other reports showing evidence that the IRA may be causing companies to reconsider their current approach to the drug development process, such as by cancelling early-stage pipeline projects, focusing

¹ Survey results on file at MassBio. We would be happy to provide the survey results to CMS, upon request.

on larger indications, developing fewer uses for existing medicines, and shifting away from small-molecule products.²

The MassBio member survey also asked about policy priorities to help maintain the biotech ecosystem as CMS implements the IRA, supplemented by qualitative input by a diverse group of executives from members. We describe these policy priorities in greater detail as part of our comments, below.

II. Section 30: Identification of Selected Drugs for Initial Price Applicability Year 2026

While MassBio understands that CMS has limited time to implement the Negotiation Program for initial price applicability year 2026, we are deeply concerned that CMS is issuing section 30 of the Guidance as “final.” The identification of selected drugs is among the most significant policies for the Negotiation Program, and many of the policies CMS outlines in the Guidance are inconsistent with the statute and likely to result in operational issues. By issuing these policies as final, CMS has denied interested stakeholders the opportunity to provide input, and further denied itself the opportunity to learn from those comments. MassBio is submitting comments in the hopes that CMS will reconsider elements of its approach going forward.

A. Section 30.1: CMS’s Qualifying Single Source Drug Definition is Overbroad and Not Supported by the Statute.

CMS is defining the term “qualifying single source drug” (QSSD) to include all dosage forms and strengths of the drug with the same active moiety (or, for biologics, active ingredient) and the same holder of a New Drug Application (NDA) (or, for biologics, a Biologics License Application (BLA))—inclusive of products that are marketed pursuant to different NDAs/BLAs. In addition, for purposes of counting the 7(drugs)/11(biologics) years that must elapse, CMS will use the earliest date of approval of the initial FDA application number assigned to the NDA/BLA holder for the active moiety/active ingredient.

CMS’s interpretation of the term QSSD is overly broad and is not supported by the statute. For both small-molecule drugs and large-molecule biological products, the underlying statute clearly sets the QSSD definition to the *singular* approval by the Food and Drug Administration (FDA) under which the product is marketed.³ The statute does not give CMS the authority to expand the statute’s focus on a singular FDA approval to a definition that encompasses multiple different FDA approvals through the addition and utilization of an “active moiety/ingredient” test.

Furthermore, this overly broad interpretation is at odds with the practical reality of the drug development process. Given the high cost to run clinical trial for a new product and the limited success rate for wholly new therapies, drugs are generally developed by initially seeking approval for and launching smaller or more limited indications—such as orphan diseases—to show proof-of-concept. Then, as the data and science advance, developers seek additional approvals for larger indications, as well as new dosage forms, strengths and formulations. This approach is consistent with the iterative approach to clinical advancement generally applied in medicine, and also mitigates some of the risk of clinical development.

² See R. Wolrath, *How the Inflation Reduction Act is already changing how biotechs do business*. Boston Business Journal (March 13, 2023); see also J. Waldrop, *Inflation Reduction Act undermines rare disease research*. Boston Herald (Feb. 28, 2023); see also D. Beasley, *Drug companies favor biotech meds over pills, citing new U.S. Law*, Reuters (Jan. 13, 2023).

³ See section 1192(e)(1) of the Social Security Act.

Because drugs are developed in this stepwise fashion, some of the most critical drugs have—over time—received FDA approval for multiple indications that continue to treat patients across multiple disease states. However, CMS’s interpretation significantly interferes with this approach by defining QSSD overly broadly, such that CMS will use the earliest approval date across an array of products grouped together by active moiety/active ingredient, in some cases grouping products approved under separate NDAs/BLAs. This will lead to a pre-negotiation period for a given product that starts *before that product was even approved*, creating a significant disincentive to pursue additional approvals, to the detriment of certain patient populations. In addition, going forward, drug developers may seek ways to obtain approval for larger indications from the outset, dampening the rate of therapeutic innovation for smaller patient populations with unmet need. This is not ideal for patients.

For these reasons, MassBio strongly urges CMS to revise the agency’s QSSD definition to instead focus on the approval standard required by statute.

B. Section 30.1.1: CMS Should Implement the Orphan Drug Exclusion in a Manner that Continues to Incentivize the Development of Rare Disease Therapies.

In the Guidance, CMS states that to be considered for the IRA’s orphan drug exclusion, a drug or biological product must (1) be designated as a drug for only one rare disease or condition under section 526 of the FD&C Act; and (2) be approved by the FDA only for one or more indications within such designated rare disease or condition. Notably, to qualify for the orphan drug exclusion, *all dosage forms and strengths and different formulations of the QSSD must meet the criteria for exclusion.*

MassBio is concerned that the narrow scope of the orphan drug exclusion, combined with CMS’s overly broad QSSD definition, creates a strong disincentive for developers to continue to develop new indications and formulations for existing orphan therapies. However, we support CMS’s commitment to “consider[] whether there are additional actions the agency can take in its implementation of the Negotiation Program to best support orphan drug development,” and urge the agency to adopt policies along these lines.

Rare diseases, as defined by the FDA are conditions that impact fewer than 200,000 patients nationwide, and are inherently under-researched, under-diagnosed, and under-treated. Although much progress has been made since the enactment of the Orphan Drug Act (ODA) 40 years ago, over 90 percent of known rare diseases do not have therapies or treatments. This scarcity in therapies is due to a variety of reasons, including the resource and time investment needed to generally design, develop and bring a drug to market,⁴ as well as the low success rate of this process.⁵ There are also plethora of challenges specific to developing drugs for rare diseases, as the low number of actual patient numbers for certain diseases makes it difficult to establish an adequately sized and diverse patient population for a clinical trial, as well as obtain the high-quality patient data necessary to evaluate clinical trial outcomes.

That said, there has fortunately been a recent surge in the development of drugs for rare disease populations,⁶ with much of this development occurring in Massachusetts.⁷ Today, 40 percent of therapies

⁴ It can take 10 to 15 years and \$1-2B for a drug to be designed, developed and approved for use in patients. I.V. Hinkson, B. Madej, E.A. Stahlberg. *Accelerating therapeutics for opportunities in medicine: a paradigm shift in drug discovery Front Pharmacol*, 11 (2020), p. 770

⁵ 90 percent of developed drugs are unsuccessful. H. Dowden, J. Munro. *Trends in clinical success rates and therapeutic focus Nat Rev Drug Discov*, 18 (2019), pp. 495-496.

⁶ The annual number of orphan drug designation requests has steadily increased from 2012 through 2016 and has remained greater than 500 annually since 2016. In 2020, the Office of Orphan Products Development received 753 new requests for designation, a 41% increase from 2019. See <https://www.fda.gov/news-events/fda-voices/rare-disease-day-2021-fda-shows->

in the pipeline are in rare disease. Furthermore, given the nature of rare diseases, therapies developed for a particular rare disease can often be the starting point in the translation of new scientific discoveries to clinical medicine. Thus, as new data emerge, developers are able to identify promising new uses, including additional orphan indications, for existing therapies. For example, many new therapies are gene-based, and each genetically defined disease is a new indication for a particular therapy.

However, these new indications still require costly clinical trials, regulatory approvals and adherence to regulatory requirements and the narrow scope of the orphan drug exclusion creates a strong disincentive to undertake these investments, even though the science is there and could benefit vulnerable populations. Furthermore, because of the limited scope of the exclusion, companies may be disincentivized from developing therapies for rare diseases to begin with, and to instead prioritize indications with larger patient populations from the outset.

MassBio urges CMS to implement the orphan drug exclusion in a way that promotes and is consistent with the underlying purposes and goals of the ODA: to create the necessary financial incentives to accelerate the development of rare disease drug development. Specifically, in addition to narrowing the agency's QSSD definition, as described above, CMS should exercise its regulatory discretion to start the pre-negotiation period for orphan drugs upon loss of the orphan drug exclusion (i.e., when the product obtains approval for a new indication for a different disease or condition), rather than when the QSSD was initially approved. This approach is within CMS's discretion to implement the statute and would shield the product from the IRA's negotiation provisions for the entire time the orphan drug exclusion applies.

III. Section 50: Negotiation Factors.

A. Section 50.1: CMS Define R&D Costs More Broadly.

The IRA directs CMS, for purposes of negotiating the MFP of a selected drug, to consider certain "manufacturer-specific data," which includes: research and development (R&D) costs; current unit costs of production and distribution; prior Federal financial support for novel therapeutic discovery and development; data on pending and approved patent applications; exclusivities recognized by the FDA and FDA applications and approvals; and market data and revenue and sales volume data in the United States. In implementing this requirement, we urge CMS to define R&D costs more broadly. In the Guidance, CMS states that it "is considering R&D costs to mean a combination of costs incurred by the Primary Manufacturer for all FDA-approved indications of a drug falling into" certain categories, which include basic pre-clinical research costs, post-investigational New Drug (IND) application costs, completed FDA-required phase IV trials, post-marketing trials, abandoned and failed drug costs, and all other R&D costs. However, CMS's proposed approach overlooks certain investments critical to drug development.

First, by focusing solely on R&D expenditures made by the Primary Manufacturer, CMS's proposed definition overlooks contributions made by the Secondary Manufacturer and others. As noted above, drug development is often a collaborative process, involving investments by both small biotech companies and larger pharmaceutical companies. This can take the form of licensing arrangements, co-promotion agreements, and other arrangements. By looking only at the expenditures made by the manufacturer that holds the NDA/BLA, CMS is ignoring a large portion of R&D costs. We also note that

[sustained-support-rare-disease-product-development-during-public#:~:text=The%20annual%20number%20of%20orphan,a%2041%25%20increase%20from%202019.](#)

⁷ D. Seiffert, *Massachusetts owns the orphan drug market. Here's the proof*, Boston Business Journal (Nov. 9, 2015), <https://www.bizjournals.com/boston/blog/bioflash/2015/11/massachusetts-owns-the-orphan-drug-market-here-s.html>.

this approach is not supported by the statute, which looks at research costs of the “manufacturer,” a term that’s defined quite broadly to refer to:

any entity which is engaged in—

(A) the production, preparation, propagation, compounding, conversion, or processing of prescription drug products, either directly or indirectly by extraction from substances of natural origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis, or

(B) in the packaging, repackaging, labeling, relabeling, or distribution of prescription drug products.⁸

CMS should therefore consider R&D spend from across the innovation ecosystem. However—contrary to CMS’s proposals in the Guidance—it should not be the responsibility of the Primary Manufacturer to collect this information from Secondary Manufacturers or others. Not only is there no statutory basis for this approach, Primary Manufacturers generally lack access to information regarding the business operations of other manufacturers, and requiring companies to share this sensitive information amongst themselves would add burden and create legal risk. Therefore, CMS should instead enter into a Negotiation Agreement with each manufacturer—including Secondary Manufacturers—to govern the submission, use, and disclosure of the data CMS needs for the Negotiation Program.

In addition, CMS’s proposed definition for abandoned or failed drug costs suggests the agency will only consider failed or abandoned product costs for products with some relation to the selected drug at issue (i.e., same active moiety, active ingredient, mechanism of action and therapeutic class). Although these categories capture many of the costs incurred in the development of a given drug, MassBio urges CMS to clarify that it will also allow manufacturers to allocate R&D costs for abandoned and/or failed research *that is not attributable to any particular product* across a manufacturer’s selected drugs. Developers often incur significant costs in the early stages of the pre-clinical discovery and development process that may not be tied to any particular product, but that were instrumental in moving the needle of scientific discovery forward and laying the groundwork for subsequent innovations that do lead to life-saving therapies. This aspect of R&D is a vital component to the larger process, and should be a material factor considered by the agency.

B. Section 50.2: CMS Should Consider Robust Data on Therapeutic.

The IRA further directs CMS to consider “evidence about therapeutic alternatives.” This includes the extent to which the selected drug represents a therapeutic advance and the extent to which the selected drug and the therapeutic alternatives address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy. CMS must also consider the FDA-approved prescribing information for the selected drug and therapeutic alternatives, and evidence on the comparative effectiveness of the selected drug and its therapeutic alternatives.

There are several factors and sources that CMS should consider in assessing a drug’s comparative effectiveness, whether it represents a therapeutic advance, or addresses an unmet need. We provide the following recommendations, and would welcome the opportunity to meet with the agency to further discuss these and other factors and sources the agency should consider as part of this assessment:

- Patient-centered definitions of value;

⁸ Social Security Act (SSA) § 1191(c)(1) (referencing SSA § 1847A(c)(6)(A), which in turn references SSA § 1927(k)(5)).

- Real-world evidence;
- Multiple-criteria decision analysis that considers multiple conflicting criteria in decision-making;
- Clinical effectiveness ratings, such as those issued by the United States Preventive Services Task Force (USPSTF); and
- Clinical compendia

We also recommend—consistent with the statutory requirement to consider FDA-approved prescribing information—that CMS focus solely on the approved indications for a given therapy.

C. Section 50.2: CMS Should Consider Data on Therapeutic Alternatives in a Non-Discriminatory Manner.

MassBio strongly supports CMS’s proposal not to use information found by CMS that treats extending the life of individuals in these populations as of lower value, for example certain uses of quality-adjusted life-years (QALYs), in the negotiation process. This policy aligns with prohibitions set forth in statute, and will help ensure that CMS is not evaluating the value of a given therapy in a manner that discredits its benefit to the neediest and most vulnerable populations. However, we are concerned that certain data sources may violate this prohibition in a discrete way, for example, by describing the research methodology without use of the term “QALY,” or by including a QALY analysis as a component of the research methodology without disclosing as much. MassBio therefore recommends that CMS disclose to manufacturers, as part of the negotiation process, all evidence that was considered by CMS in developing the initial MFP offer. A manufacturer can then use that information to ensure that any such data that involves QALYs and other similarly problematic metrics—either directly or indirectly—are not included in the manufacturer’s counteroffer.

IV. Section 60: Negotiation Process

A. CMS Should Adopt Certain Guiding Principles for Implementation of Negotiation Provisions to Promote Innovation.

As CMS proceeds with implementation of the Negotiation Program, MassBio urges the agency to pursue an approach that creates the greatest degree of certainty for developers by adopting a predictable, transparent methodology for applying the relevant negotiation factors, which should then be updated over time to recognize the value of continued innovation. As explained above, investment in the drug development process and the innovation ecosystem is significantly impacted by the long-term market dynamics at play. Thus, to enable developers and their investors to make informed investments today, CMS’s methodology should reflect the value that a product provides over its lifecycle and create incentives to invest in new therapeutic areas with unmet need.

For example, in the context of determining whether a selected drug represents a therapeutic advance as part of the negotiation process, MassBio urges the agency to consider the recent renaissance in the development of small-molecule drugs, which are increasingly complex, and to reject the common misconception that small-molecule drugs are not inherently innovative, or as innovative as biologics.⁹ CMS should similarly reject the notion that small-molecule drugs are less innovative or represent less of a therapeutic advance in the treatment of disease. Furthermore, it should be noted that small molecule

⁹ H. Boehm, *The Renaissance of Small Molecule Drug Discovery*, Pharmacy Times (Aug. 9, 2022), <https://www.pharmacytimes.com/view/the-renaissance-of-small-molecule-drug-discovery>.

drugs are often reproduced as generics, once the original drug patent expires, which can in turn further increase the availability of treatment options for vulnerable patient populations. However, as mentioned above, recent reports suggest that the IRA may be causing developers to shift away from small-molecule products to begin with. If this disincentive leads to less development of small-molecule drugs, it follows that it will also negatively impact the availability of generics, to the detriment of patients.

Thus, to in order to preserve access to small-molecule products and biologics alike, CMS should adopt an approach that ensures that maximum fair price (“MFP”) is set at or near the ceiling price for products that represent a therapeutic advance or address an unmet need. This approach would both create predictability and enable long-term investment in innovative small-molecule products as well as biologics. This will be especially important during the early years of the Negotiation Program, while there is significant uncertainty and a very short window for implementation. During this time, CMS can and should err on the side of mitigating against the potential harm resulting from the disincentives created by the program’s framework.

In that vein, CMS should also ensure that application of the negotiation factors is designed to promote health equity and reduce health disparities. Indeed, under the IRA, CMS must consider “the extent to which the selected drug and the therapeutic alternatives to the drug address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy.” CMS can do this by placing greater weight on the promotion of health equity and reduction of health disparities, which are accomplished in part by creating and maintaining incentives for investment in therapies that address unmet need for underserved patient populations, including patients suffering from rare disease.

B. CMS Should Continually Monitor the IRA’s Impact on the Innovation Ecosystem.

As mentioned above, in early 2023, MassBio surveyed its membership regarding the IRA’s immediate impacts, and member perspectives regarding certain regulatory and legislative policies that could mitigate those impacts. MassBio plans to continue to survey our membership and perform other data-driven approaches to monitor the impact of the law, and we hope to have the opportunity be a resource for CMS as it begins to track the impact of the IRA.

Likewise, as CMS proceeds with implementation of the law, MassBio urges the agency to similarly prioritize building the necessary infrastructure to track the impact of the IRA on the innovation ecosystem. This will be vital given the long-standing relationship between innovation and increased access to life-saving therapies, and the need for the agency to “do no harm” in the implementation of this new program. For instance, CMS could track the following metrics, using CMS’s own data and certain data available from the FDA, to assess the IRA’s impact over time.

- Number of new technology add-on payment (NTAP) applications for drugs and biologics;
- Requests for pass-through status under the Hospital Outpatient Prospective Payment System (OPPS);
- Number of new NDCs in average sales price (ASP) reporting data;
- Number of NDA/BLA submissions (tracking proportion of small-molecule vs. large-molecule over time);
- Number of supplemental BLA/NDA submissions;
- Number of applications for orphan drug designation (ODD);
- Percent of products with an ODD that are approved by FDA;
- Number of applications for breakthrough therapy designation;

- Number of applications for fast-track designation; and
- Number of applications for regenerative medicine advanced therapy designation.

We further urge CMS to publicly report these data to inform both the public and policymakers in Congress, and to establish a dynamic framework pursuant to which significant decreases in the metrics captured above trigger reconsideration of the negotiation process implemented by the agency.

V. Conclusion

MassBio thanks CMS for your consideration of our comments. As the IRA will have a significant impact across our diverse membership, we would appreciate the opportunity to meet with CMS to discuss these comments and other IRA-related issues of interest to our members.

Best regards,

A handwritten signature in black ink, appearing to read "Kendalle O'Connell", with a long horizontal flourish extending to the right.

Kendalle Burlin O'Connell, Esq.
CEO & President
MassBio

www.mckesson.com

April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Subject Line: Medicare Drug Price Negotiation Program
200 Independence Ave., SW
Washington, DC 20201

Submitted via email: IRARebateandNegotiation@cms.hhs.gov

**Re: Medicare Drug Price Negotiation Program: Initial Memorandum,
Implementation of Sections 1191 – 1198 of the Social Security Act for Initial
Price Applicability Year 2026, and Solicitation of Comments**

McKesson Corporation ("McKesson") is pleased to provide comments on the Centers for Medicare and Medicaid Services' ("CMS") initial guidance on the implementation of the Medicare Drug Price Negotiation Program ("Negotiation Program"). We appreciate the opportunity to share our perspectives on how CMS can achieve its goals of improving access to affordable, innovative treatment with minimal patient, provider, and supply chain disruption. Our comments focus on the foundational aspects of the new program and the more immediate considerations impacting effectuation of Part D maximum fair prices ("MFPs") across the pharmaceutical value chain.

About McKesson

McKesson is a global leader in healthcare supply chain management solutions, retail pharmacy, community oncology and specialty care, and healthcare information solutions. McKesson partners with pharmaceutical manufacturers, providers, pharmacies, governments, and other organizations in healthcare to help provide the right medicines, medical products, and healthcare services to the right patients at the right time, safely and cost-effectively. As a mission-driven company, McKesson is focused on working with customers and partners to advance health outcomes for all. McKesson strives to ensure that its views on improving healthcare prioritizes what's best for the patient. Its public policy platform is driven by the core belief that the **Patient Comes First**.

McKesson is also a leader in physician and pharmacy technology solutions. CoverMyMeds® solutions seamlessly connect the healthcare network to improve medication access, thereby increasing speed to therapy and reducing prescription abandonment. CoverMyMeds' network includes 75% of electronic health record systems (EHRs), 50,000+ pharmacies, 750,000 providers and most health plans and pharmacy benefits managers (PBMs). Ontada®'s oncology technologies, including the oncology-specific iKnowMedsm electronic health record (EHR), are utilized at the point of care and support clinical and operational excellence, generating claims, reimbursement, and labs oncology data across more than 2,700 oncology providers in 40 states.

General Comments

We share the Administration's belief that *all* patients must have access to affordable medicines and care to improve outcomes and reduce both patient and health system costs. McKesson's unique 360-degree view of the healthcare system offers a distinctive vantage point to examine key considerations impacting the effectuation of the MFP. Our industry-leading subject matter experts have carefully examined the initial guidance and engaged key partners across the pharmaceutical value chain to explore the data and payment processes critical to the effectuation of the MFP. We recognize that seamless effectuation of the MFP is central to the success of the new Negotiation Program. We appreciate the opportunity to share our perspective on how CMS may advance a minimally disruptive process to meet its goals.

First, it is important to recognize that CMS' proposed dual use of the MFP as a payer reimbursement benchmark (i.e., Part D negotiated price) and pharmacy acquisition benchmark is a significant departure from current practice. Today, for pharmacy benefit drugs (e.g., Part D), these two processes—acquisition from wholesalers and reimbursement by Part D plans—are not linked and represent distinct contractual agreements. Additionally, adjustments to acquisition costs are made through the wholesaler *prior* to the drug being dispensed and apply to all drugs a pharmacy may purchase, regardless of the payer type (e.g., Medicare, Medicaid, commercial, cash-pay). The transactions contemplated by CMS better align with manufacturer 'refund' transactions, which may include post-dispense retrospective adjustments to reimbursement, but would not work with pre-dispense prospective adjustments to acquisition cost.

Second, we appreciate that CMS intends to "leverage existing mechanisms" to ensure the MFP is made available to MFP-eligible individuals and dispensing entities. While we think the private sector can be a solutions partner, this is only effective if CMS plays an active role in defining and governing core operations necessary to effectuate the MFP. Experience shows that when left to solve common business challenges individually, private sector entities will implement unique policies and processes relevant only to their own business models, which fuels market confusion, fragmentation, and disruption.

Last, we appreciate that while the statute places primary responsibility of MFP availability on manufacturers, CMS has the authorities and an inherent responsibility to ensure new programs and benefits are implemented with the appropriate level of transparency, oversight, and compliance protections for beneficiaries, pharmacies, and the Medicare program.

Specific Comments: Minimizing Disruptions

We believe the following are vital to the success of the Negotiation Program and MFP effectuation:

- **CMS must define, construct, and oversee core functions of the data and payment processes critical in effectuating the MFP across all stakeholders.** CMS guidance and oversight is critical to building trust across all stakeholders and mitigating potential barriers due to competing business interests and misaligned incentives.
- **CMS must require manufacturers and impacted entities to adopt a singular, standardized approach.** Consistency will ensure that pharmacies are not forced to navigate manufacturer-specific programs with varying requirements. Effectuating the MFP should not come at the cost of diverting pharmacy time, resources, and attention

away from patient care or adding undue financial / administrative burden to already-stretched pharmacist workforce capacity.

- **CMS must provide detailed operational guidance and resources to support uniformity, including minimum data standards.** The Inflation Reduction Act (IRA) requires CMS to implement the Negotiation Program “by program instruction or other forms of program guidance.” CMS must consider the unintended consequences of erring on the side of too little—rather than too much—guidance.
- **CMS must hold pharmacies harmless and reduce administrative and financial risk.**
 - **Pharmacies should not be on the hook to “prefund”** the retrospective MFP-model and face “pay and chase” hurdles as they pursue payment for the “MFP refund.” CMS should explore alternative opportunities to prefund transactions.
 - **CMS should require the MFP refund be processed in the same manner and timeframe as the Part D manufacturer discounts.** This approach would align all claims-related transactions and ensure timely 14-day payment post-dispense.
 - **CMS must reframe the “providing access to the MFP” definition** from “ensuring that the amount paid by the dispensing entity for the selected drug is *no greater than the MFP*” to “ensuring that the amount reimbursed to the dispensing entity for the selected drug is *no less than the MFP*.” Disassociating the MFP refund calculation from acquisition cost (which is confidential, highly variable across pharmacies, and prone to dynamic change even for a given pharmacy) will allow entities other than the pharmacy to calculate the MFP refund. **Making the MFP refund “knowable and portable” is the start to automating the effectuation process.**

The remainder of this document provides an overview of the key considerations we believe to be critical across stakeholders, offers specific comments on leveraging the existing supply chain, and presents tactical comments on better effectuating the MFP.

Overview: MFP Effectuation: Aligning Interests and Operational Imperatives¹

As we examined the operational considerations for effectuating the MFP, McKesson identified guiding principles to bridge the common goals across key stakeholders. We also explored operational ambiguities remaining from the initial guidance that must be addressed prior to program implementation.

Patients must have timely and robust access to critical medicines and benefit from lower cost sharing from MFP at the point of sale (“POS”).

Medicare must provide robust access to innovative treatments while lowering costs and safeguarding program success.

Pharmacies² must be held harmless for timely payments and face minimal administrative burden and financial risk.

Manufacturers need timely, complete, and accurate data reporting critical to ensuring the auditability of MFP financial transactions and compliance with program requirements (e.g., manufacturer agreement, non-duplication of 340B discounts).

Wholesalers must provide timely and uninterrupted delivery of critical medicines to customers.

340B Covered Entities must have access to the lowest acquisition cost – MFP or 340B ceiling price.

Technology entities must access shareable, portable data to support diverse stakeholders across the supply chain.

Common Guiding Principles Across All Stakeholders

- Ensure minimal disruption to current product, data, and financial flows
- Leverage existing roles and capabilities, where possible
- Be selective when introducing new entities and process
- Have necessary guidance and resources for a coordinated and consistent approach

Operational Imperatives: Framework Overview and Sample Questions

Identify Least Disruptive Approach: Between prospective versus retrospective, which approach minimizes pharmacy administrative and financial risk? Which mitigates inventory challenges and diversion risk?

Better Define MFP Effectuation and Intersection with 340B: How can the process be automated to ensure timely pharmacy payment? How should the “MFP refund” be defined and calculated? Who should prefund the financial transactions? How is the process impacted by 340B?

Determine Optimal Roles Based on Real-World Solutions: Should a single entity manage both data and financial transactions? Should these entities be governed and paid for by CMS, by manufacturers, or by an independent third party?

¹ Content not meant to be exhaustive, but reflective of priority needs.

² Please note that we often use the term “pharmacy” as shorthand for all dispensing entities that may be impacted under the Negotiation Program.

Specific Comments: Leveraging Existing Supply Chain Capabilities

McKesson believes there are numerous pathways through which the MFP may be effectuated. CMS' willingness to be an active partner in the process and in the provision of detailed direction, standardization, and automation will impact feasibility, timing, willingness of stakeholders to partner, and ultimately a successful program. The barriers to creating new operational processes are not insurmountable and can be done by relying on existing infrastructure and business relationships across the primary stakeholders in the supply chain (i.e., pharmacy, plan, pharmacy switch, manufacturer). However, private-sector leaders need the Administration's guidance to ensure new solutions do not unduly fragment the supply chain, reduce efficiency, or lead to disruption.

CMS must also safeguard against the competing business priorities and misaligned incentives that may create undue burden on pharmacies. Pharmacies are at the epicenter of effectuating the MFP and will be required to navigate significant changes to their drug management processes and economics. They should not *also* be tasked with taking on the brunt of the administrative and financial risk. For example, without CMS intervention, pharmacies may be forced to take on primary responsibility of identifying MFP-eligible patients at the POS, confirming dispensing of MFP-selected drugs, calculating and submitting the MFP refund, 340B reconciliation, financial reconciliation, and related compliance requirements. While we appreciate CMS' intent to prohibit manufacturers and their contracted partners from charging fees for the retrospective MFP payment process, this will not fully insulate pharmacy risk, nor does this account for the costs and burden of the ancillary activities critical to supporting MFP effectuation. It is not practical or appropriate to place the greatest administrative and financial risk on pharmacies, especially independent pharmacies who have limited resources to manage such sweeping reforms.

Minimally Disruptive Pathway

The least disruptive approach in effectuating the MFP is to leverage systems and entities already performing similar roles. The Medicare Coverage Gap Discount Program (CGDP) and use of a CMS-financed and governed third-party administrator (TPA) is a trusted and proven approach. In the CGDP, manufacturer discounts are seamlessly effectuated at the POS, in real time and within workflow. The model also allows for regular data and financial reconciliation across the key stakeholders in the Part D claims and reimbursement system (pharmacy, Part D plan, CMS, manufacturer, patient). CMS has already indicated that this same model will be used to operationalize the new Manufacturer Discount Program ("MDP") that will be effective under the new Part D benefit starting in 2025. We urge CMS to examine the potential overlapping needs and functions necessary to effectuate the manufacturer discount relative to the manufacturer MFP refund. Synergies may mitigate costs of deploying a new TPA model just for MFP effectuation. This model also mitigates pharmacy financial risk by removing their burden to prefund the MFP refund. We urge CMS to explore financing models that would allow manufacturers to seamlessly pay MFP refund amounts to pharmacies at the POS.

Defining Critical Functions

In determining a path forward, it is important to first determine the key functions or capabilities needed to process the core transactions, and the ability of entities already involved with these transactions to expand their role to address the new requirements to effectuate the MFP.

Based on our understanding of similar flows in the supply chain today, we believe there are two distinct needs in effectuating the MFP: Data Facilitation and Payment Facilitation.

Data Facilitation

The statute mandates that manufacturers make the MFP for selected drugs available to both MFP-eligible individuals and dispensing entities. Per CMS' initial guidance, this requires the manufacturer to ensure that the selected drug was dispensed to eligible patients and that the pharmacy's purchase price is no greater than the MFP. When not purchasing the selected drug at MFP, which is most likely, dispensing entities will need an MFP refund from the manufacturer. Additionally, manufacturers must guard against 340B discount duplication and ensure covered entities are able to purchase selected drugs at the lesser of the MFP or 340B ceiling price.

These requirements necessitate the coordination and reconciliation of several disparate data elements. Examples of core data transactions include, but are not limited to:

- ✓ Part D Verification: Determine patient and drug MFP eligibility
- ✓ Identify 340B transactions that would not be MFP-eligible
- ✓ Calculate MFP refund
- ✓ Determine total pharmacy payment across responsible entities: patient, Part D plan and manufacturer

Payment Facilitation

As noted above, as part of the MFP effectuation process, manufacturers may owe pharmacies an MFP refund that must be reconciled, at the claim level, against dispensing of the MFP drug. Examples of core financial transactions include, but are not limited to:

- ✓ Pay pharmacy amount determined through data facilitation process
- ✓ Manage all related transactions and needed true-ups (reversal of refund if claim reversed, post-refund 340B ceiling price reconciliation)
- ✓ Coordinate financial transaction to claim transactions

Leveraging Existing Supply Chain Capabilities

As noted earlier, there are numerous pathways in which the MFP may be effectuated but additional direction and guidance is needed from the Administration. As we examined the opportunity to leverage existing supply chain capabilities, we identified attributes necessary for entities to function as a Data and Payment Facilitator.

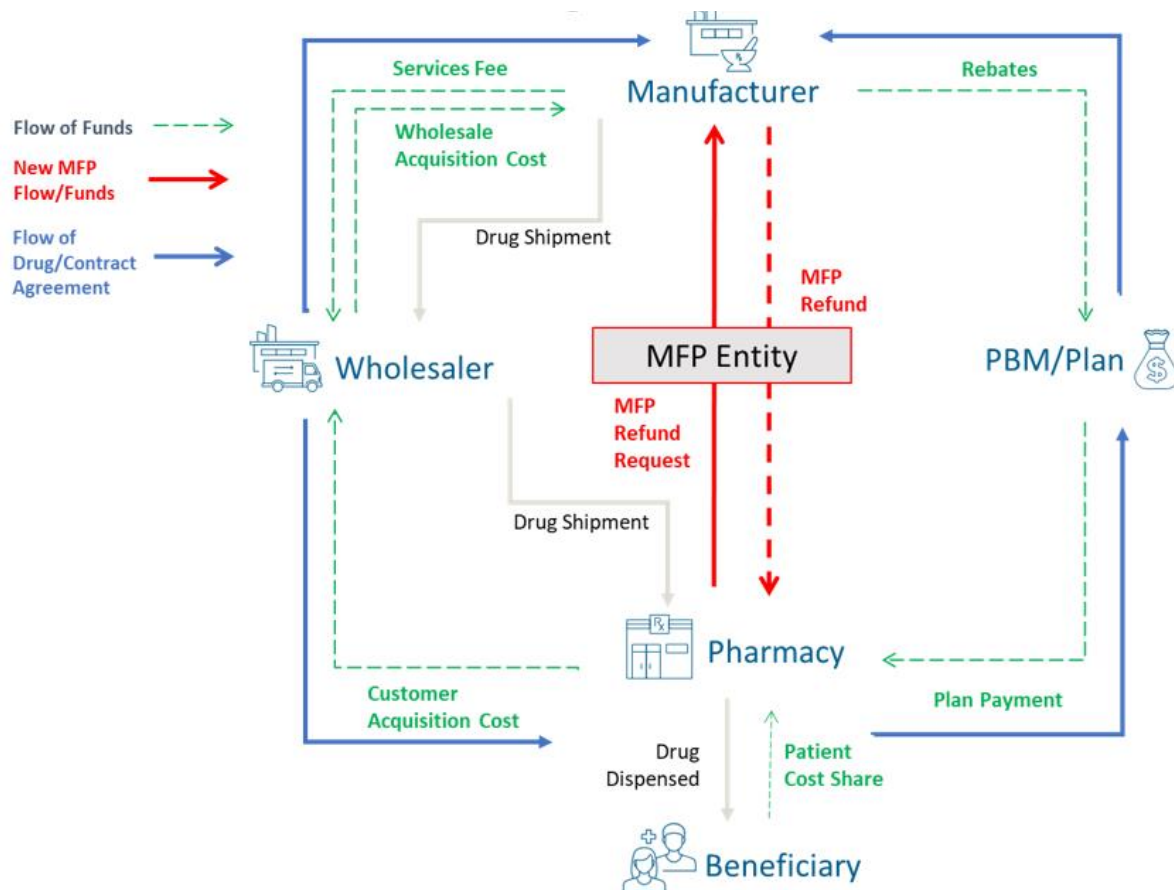
Data Facilitator	Payment Facilitator
<p>Entities best positioned for this role</p> <ul style="list-style-type: none"> ✓ Can validate Part D eligibility ✓ Already have access to Part D claims data in their current workflow ✓ Already have or could be granted access to 340B data to enable identification of ineligible claims for 	<p>Entities best positioned for this role</p> <ul style="list-style-type: none"> ✓ Able to link financial payments claims as critical to ensuring compliance of MFP effectuation ✓ Already function as pharmacy claims, billing, and operating solution

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Data Facilitator	Payment Facilitator
MFP, and operationalize true-ups when MFP is lower	✓ Able to identify and initiate refund automatically within workflow

Ideally, a single entity would serve both roles, but it is also plausible to split those roles between two different entities. For the payment facilitator role, there are two possible entities that are currently part of financial flows to pharmacy – the Part D plan or the pharmacy switch. For the data facilitator role, possible entities could be Palmetto (CGDP TPA), the pharmacy switch or a new data clearinghouse.

Figure 1. Intersection of the MFP Entity in Current Supply Chain



It is important to note that the success of any private sector solution or partnership will require additional guidance and direction from the Administration. Critical areas for consideration:

- Define roles and responsibilities for key activities and transactions in the MFP effectuation process (e.g., Part D plan required to verify MFP eligibility, pharmacy required to determine refund amount if based on purchase price)

- Clarify which entities can play a role in effectuating the MFP based on required capabilities (e.g., only Health Insurance Portability and Accountability Act (HIPAA) covered entities are able to manage claims-based level transactions)
- Define minimum data standards for core transactions (e.g., refund request must include claim number, NDC, units dispensed, etc.)
- Clarify financial accountabilities across stakeholders to mitigate unintended consequences and cost shifting to pharmacies

Specific Comments: Better Define MFP Effectuation and Intersection with 340B

Pharmacy Reimbursement vs. Acquisition under MFP

Current Considerations: Pharmacies purchase drugs agnostic to patient insurance designation. Pre-POS discounts from manufacturer to pharmacy are highly uncommon in the Part D flows today. Therefore, wholesaler chargebacks are the exception, not the rule, in Part D scripts that flow primarily through retail pharmacies and specialty pharmacies. Pharmacy acquisition cost is based on contractual agreements between wholesalers and the purchasing pharmacy entity; they are not driven by payer or patient designation.

MFP Considerations: Per the initial guidance, CMS intends to require that manufacturers of selected drugs provide access to the MFP in one of two ways: (1) prospectively by ensuring the price paid by the dispensing entity at acquisition is “no greater than the MFP;” or (2) providing a retrospective reimbursement between the pharmacies’ acquisition cost and the MFP. See Figure 2 below.

Figure 2. Understanding Acquisition Dynamics Based on CMS Example

	Prospective		Retrospective
	Some Inventory Bought as Usual	Some Inventory Bought at MFP Price	All Inventory Bought as Usual
Pharmacy purchases MFP-eligible medication bottle for...	\$100	\$80	\$100
MFP-eligible patient identified with \$0 cost-sharing	Medication cannot be dispensed to qualifying Part D patient ... even if MFP acquired supply runs out	\$0	\$0
The MFP applied to this selected package is...		\$80	\$80
Part D plan doesn't negotiate discount below acquisition or the MFP. Negotiated price...		Equals MFP (\$80) + dispensing fee	Equals MFP (\$80) + dispensing fee
Plan + Patient Pays Pharmacy		\$80 + dispensing fee	\$80 + dispensing fee
Pharmacy Owed (Purchase \$ - MFP)		\$0	\$20 “MFP-refund”

A prospective MFP approach creates undue burden for pharmacies by requiring them to manage dual inventories and also creates diversion / financial risk for manufacturers due to lack of visibility, transparency, and auditability of appropriate use of MFP-priced product for eligible Part D enrollees.

Under this approach, pharmacies would be required to acquire some drugs at the “no greater than the MFP” amount and others under their standard acquisition rates (e.g., wholesale acquisition cost minus [WAC-minus]). Split billing and management technology solutions typically used by 340B covered entities are unlikely to solve challenges unique to community pharmacy (e.g., limited space to manage dual physical inventories).

A retrospective MFP approach is the least disruptive for pharmacies and for manufacturers but requires CMS to implement a transparent and consistent process to facilitate the “MFP refund.”

Under this approach, pharmacies would continue to acquire all of their drugs under their standard acquisition rates (and contracts). The retrospective approach allows pharmacies to more effectively manage their drug supplies and ensure timely access for patients. It also allows manufacturers to receive granular, transparent, and timely data on eligible transactions and to validate the MFP refund owed to dispensing pharmacies. It does necessitate provision of an “MFP refund,” which, if not implemented with the necessary safeguards, may place undue financial risk and administrative burden on the pharmacy.

Pharmacies should not be on the hook to “prefund” the retrospective MFP model and face “pay and chase” hurdles as they pursue payment for the “MFP refund.”

Numerous challenges make this the least desirable and reliable option for pharmacies, particularly independents already facing economic and cash flow challenges, which will be exacerbated in the post-DIR reform landscape. First, without a clearly defined and standardized process, pharmacies may be forced to navigate different refund programs with varying manufacturer requirements. Second, use of actual acquisition cost to determine the refund amount places the burden on pharmacies to calculate, submit, and justify the refund, creating uncertainty in payment. Additionally, sharing of proprietary pharmacy acquisition data may impact competitive market dynamics. Third, manufacturers and pharmacies do not typically exchange data or dollars directly. Discounts may be contracted between the two entities but are usually effectuated by the wholesaler. Pharmacy payments through manufacturer cost-sharing programs are usually effectuated through pharmacy switch-based solutions. CMS currently effectuates CGDP discounts through partners it has contracted with and oversees, namely Part D plans and Palmetto (the TPA of the CGDP). While Part D plans may be able to play the role of payment facilitator, they would not be able to play the role of the data facilitator as they lack access to robust and timely 340B data. Moreover, if Part D plans were to play the role of data facilitator, it would be quite concerning to other stakeholders in the supply chain due to the opaqueness of the PBM model and misaligned incentives that could exacerbate financial pressures on pharmacies and manufacturers.

CMS should explore alternative ‘prefunding’ pathways that will minimize both pharmacy administrative burden and financial risk.

Notwithstanding outstanding questions regarding CMS authorities and funding pathways, we think it is vital that CMS have direct oversight of the MFP effectuation process and, specifically, that CMS govern the necessary data and financial flows. CMS is expected to terminate the CGDP under the new Part D benefit. However, the new MDP is expected to be managed in a

similar manner. Appreciating the limitations of using the current CGDP partners to perform the MFP process, we nonetheless believe CMS can use a similar model to effectuate the “MFP refund” but utilize alternative funding and payment mechanisms to mitigate resultant overburdening of Agency resources.

Ascertain MFP Eligibility

Current Considerations: Today, patient insurance status and drug choice does not impact pharmacy acquisition costs. They do, however, impact the pharmacy’s plan payment and patient out-of-pocket cost sharing.

MFP Considerations: Per the initial guidance, CMS intends to leverage existing mechanisms to ensure the MFP for selected drugs is made available to MFP-eligible individuals and their dispensing entities. Existing mechanisms fail to automate the necessary processes and create operational hurdles that limit the seamless initiation and execution of the “MFP refund.”

CMS must automate the MFP eligibility process and enable seamless identification of “MFP refund” eligible claims at the POS.

Per the initial guidance, CMS indicates that the combination of the RxBIN and RxPCN will enable pharmacies to identify MFP-eligible patients at the POS. CMS must also ensure selected drugs are easily identifiable based on the range of applicable National Drug Codes (NDCs). Further, rather than leave these mappings to pharmacies and their technology vendors, CMS should automatically flag claims that meet the core requirements (MFP-eligible individual and MFP-selected drug). This will ensure pharmacies are made aware in real-time that the “MFP refund” process should be initiated as part of the initial claims adjudication process.

Unrelated to the “MFP refund” process, we note that pharmacies will continue to rely on Part D plans to accurately reflect MFP-adjusted cost sharing as appropriate. This determination becomes more complex at the POS if the patient is also enrolled in the plan’s cost-sharing smoothing program. CMS must ensure that this information is readily available at the POS and that data standards and pharmacy systems allow for the exchange of this information.

Determining Payment Responsibilities

Current Considerations: Today, the pharmacy switch enables pharmacies and plans to automate the real-time flow of billing transactions, streamline the workflow process, resolve claims submission discrepancies that cause payment delays, and help ensure accurate and timely reimbursement to the pharmacies. When a patient presents a script at the pharmacy counter, the switch routes the billing claim from the pharmacy to the plan for adjudication, and then delivers the plans payment response back to the pharmacy in real-time. Based on this response, the pharmacy knows it will receive its full compensation under its contract with the plan and can track the payment due from the plan versus the out-of-pocket cost sharing for the patient based on the plan’s benefit design.

Under the current CGDP, manufacturers are required to provide eligible beneficiaries in the Part D coverage gap access to discounted prices for brand drugs at the POS. Today, Part D plans automatically include the manufacturer-required discount amount as part of the plan’s payment obligation. The manufacturer discount obligation is seamlessly integrated into existing pharmacy claims and payment processes. The pharmacy knows its full compensation amount for the

submitted claim at the POS. The pharmacy knows it will be paid in full by all entities within the standard 14-day claims adjudication process. Manufacturers repay Part D plans through the CGDP TPA (Palmetto). CMS, Part D plans, and manufacturers reconcile financial transactions independently without disrupting patient access or pharmacy economics.

MFP Considerations: Per the initial guidance, CMS indicates that it will define “providing access to the MFP” as ensuring the dispensing entity’s acquisition cost is no greater than the MFP. As such, in effectuating the “MFP refund,” CMS intends to require manufacturers to reimburse dispensing entities the difference between their acquisition cost and the MFP. Separating the MFP financial transaction from existing real-time Part D transactions will create significant disruptions for pharmacy (e.g., uncertainty in full payment at the POS, revenue cycle management hurdles).

A retrospective MFP approach only works if we can create an automated, transparent, and predictable process for ensuring timely payment of the “MFP refund.” A standardized approach will mitigate pharmacy burden, and ensure manufacturers have timely access to data to ensure compliance with program requirements. Existing solutions can only be leveraged if we automate the “MFP refund” determination process as is done today with other pharmacy payment responsibility determinations.

In order to automate the “MFP refund” process, the refund amount must be “knowable and portable” – necessitating use of a standardized and transparent calculation (i.e., WAC minus MFP).

As noted earlier, CMS intends to require that manufacturers reimburse dispensing entities the difference between their acquisition cost and the MFP. We appreciate CMS’ intent to “make pharmacies whole” but believe use of acquisition cost as the benchmark to determine the “MFP refund” is problematic and places undue burden on pharmacies. Only the pharmacy knows its actual acquisition cost, and many may not be able to make this determination in a timely manner or at the unit levels necessary to determine the “MFP refund.” Wholesalers have a partial view into pharmacy acquisition cost, as they only know the price at which they sold the drug to the pharmacy. However, there can be additional discounts paid directly from the manufacturer to the pharmacy that could be proprietary and not transparent to wholesalers. There also could be thousands of different acquisition costs for the same drugs as each pharmacy in the United States has different contract terms with wholesalers and manufacturers. Finally, this would expose proprietary pharmacy acquisition costs to other entities in the industry.

WAC may be used as a proxy for acquisition cost as it is generally accepted that brand drugs are acquired at or near this transparent and publicly available benchmark. Use of a WAC minus MFP calculation would streamline the process and allow multiple entities across the supply chain to calculate and apply the refund amount. WAC and MFP are both publicly available and, as such, create a predictable and auditable MFP refund amount for all stakeholders, including pharmacies, manufacturers, and CMS.

Payer Claims and MFP Refund Requests

Current Considerations: As noted earlier, the pharmacy switch enables pharmacies and plans to automate the real-time flow of billing transactions. The CGDP process shows how

manufacturer-discount obligations can be seamlessly integrated into these workflows and transactions, thus minimizing pharmacy administrative burden and financial risk. Inclusion in established claims processes also ensures that pharmacies will be paid in full by all entities within the standard 14-day claims adjudication process.

MFP Considerations: In the initial guidance, CMS notes that manufacturers must reimburse pharmacies the MFP refund within 14 days. However, there is no clarity on when the clock starts or what hoops pharmacies may be required to jump through to get the refund. Without specificity in how the refund should be operationalized within 14 days, industry alignment on how best to utilize existing solutions is unlikely.

“MFP refund” payment standards should align with established Part D payment requirements – within 14 days of claims adjudication.

Pharmacies should not have to navigate financial uncertainty and cash flow hurdles due to the Negotiation Program or perceived operational challenges by CMS, manufacturers, or other supply chain entities. Community pharmacies continue to face economic challenges due to reduced reimbursements and the evolving payer / PBM landscape. Divorcing the “MFP refund” from the standard payment processes and revenue cycle management solutions opens the door for DIR 2.0 claw backs. Precedent exists for CMS to mandate and support operationalization of manufacturer discounts within the CGDP within these same timeframes.

340B Reconciliation

Current Considerations: 340B patient and claims identification is an ongoing challenge. Without binding direction from HHS, stakeholders tackling the same challenges have operationalized a wide array of solutions. This 340B data fragmentation across multiple entities prevents the identification of 340B claims at the POS and makes post-POS reconciliation challenging. While standards issued by the National Council for Prescription Drug Programs (NCPDP) allow for use of a 340B modifier, it is intended to be used at the POS. Nothing prohibits the pharmacy from reporting this information post-POS, and the lack of clarity and length of time to make such determinations do not make use of this modifier practical or reliable.

Contract Entities Have Significant Latitude in Determining 340B Eligibility: The regulatory definition of “patient” allows for wide interpretation. So, while preliminary eligibility may occur by matching the patient’s prescription at a contract pharmacy to a prescriber and encounter at a 340B covered entity (CE), additional “rules” are applied after the POS to maintain 340B compliance. These “rules” or “algorithms” vary by CEs and their perspectives on issues such as 340B compliance, optimization of the program, etc. Examples of additional qualifying criteria: evaluation of referral pathway and alignment of diagnosis with prescription.

340B Eligibility May Not Translate into Use of 340B Discount: Covered entities typically use 340B TPAs as an intermediary between covered entities and contract pharmacies for a range of services, including but not limited to: identifying 340B-eligible prescriptions; managing financial payments between both entities; managing inventory; and performing compliance checks. The 340B TPA is also one of the few, if not only, entities that is able to determine if 340B eligibility was pulled through and replenished as a 340B ceiling price acquired product. For example, a contract pharmacy that dispensed a seasonal medicine may choose not to “replenish” a product months later if it is not likely to be used until the following season.

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MFP Considerations: The IRA creates statutory dependencies on the 340B Program relative to both effectuating the MFP process within the supply chain, as well as for calculating inflationary rebate calculations for both Part D and B drugs. While the dependencies are different, they both underscore the need to describe how the current 340B claims adjudication process works in the supply chain today, and the issues that must be solved for in implementation, to ensure 340B claims are utilized as prescribed by statute.

CMS clarifies for the purposes of effectuating the MFP and non-duplication of 340B discounts, that the manufacturer must ensure a covered entity's acquisition cost is the lesser of the MFP or 340B ceiling price.

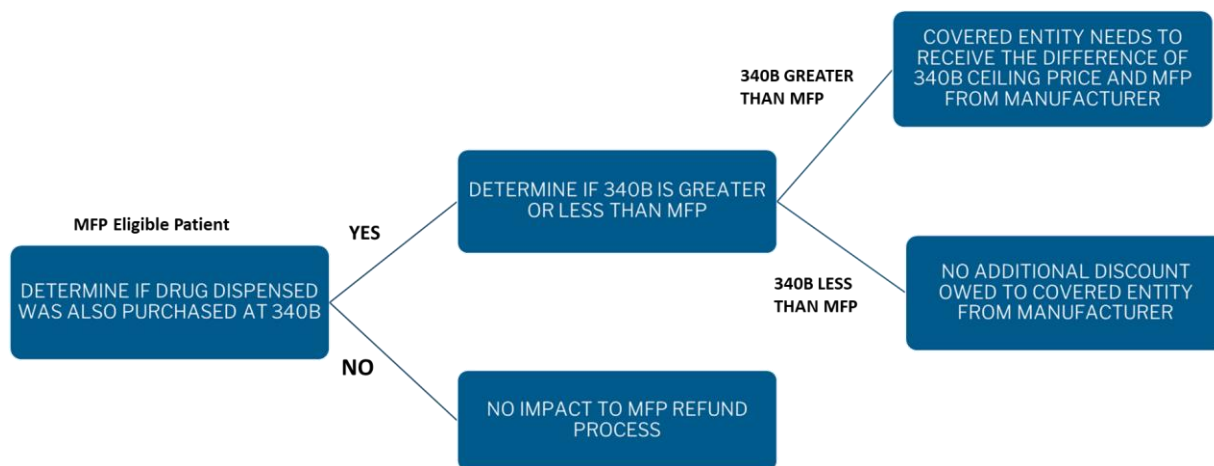
340B unit identification should remain a post-POS designation.

It is impractical to force designation at the POS when there is considerable variability in identification of the 340B unit.

For the purposes of MFP reconciliation, CMS should identify drugs whose 340B ceiling price is lower than the MFP at the POS to flag these claims for prioritized 340B eligibility determination and pull through.

The intersection between MFP and 340B creates significant complexities in dollar flows between both pharmacy and manufacturer (and the plan as well, if they are part of the MFP refund). CMS should consider the below challenges as they develop the process for 340B units that are also MFP eligible. Foundational questions that will need to be solved are included in Figure 3.

Figure 3. Understanding Complexities of MFP and 340B



Challenges to consider

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As stated above, the identification of a 340B transaction is not known at the POS. In all scenarios, the patient's cost sharing must be off MFP at the POS. In addition, for pharmacies to be held harmless and paid within 14 days, the MFP refund must be paid at the time of reimbursement. As 340B is generally not known until well after 14 days, there will need to be a financial true-up, in which pharmacies will need to repay manufacturers for the MFP collected but should not have as it was 340B unit. The repayment true-up to manufacturers will be determined if 340B is greater or less than MFP.

CMS should create a robust true-up process for manufacturers to ensure there are no duplicate discounts for MFP eligible drugs that were purchased at a 340B ceiling price.

Conclusion

McKesson thanks CMS for its consideration of these comments and for recognizing our shared interest to provide all patients access to affordable medicines and care. To further our common goal to find solutions that bring minimal disruption to the pharmaceutical supply chain, we urge CMS to take a leadership role and commit to resolving the following key issues:

- Defining, constructing, and overseeing core functions of the data and payment processes critical in effectuating the MFP across all stakeholders;
- Investing in the resources of both a data and payment facilitator, overseen by CMS, to ensure the integrity of supply chain data and the MFP program itself;
- Requiring manufacturers and impacted entities to adopt a singular standardized approach;
- Providing detailed operational guidance and resources to support uniformity, including minimum standards;
- Ensuring that pharmacy is held harmless without elevated administrative and financial risks;
- Reframing the definition of "providing access to the MFP" to enable workable solutions; and
- Solving the critical intersections between 340B and MFP to ensure the integrity of both programs.

We look forward to future opportunities to collaborate with the Agency as it implements and oversees the Negotiation Program. Should you have questions about our comments or need further information, please contact Fauzea Hussain, Vice President of Public Policy, at Fauzea.Hussain@McKesson.com.

Sincerely,



Pete Slone

Good Morning,

I am writing in response to the request for comments regarding the Inflation Reduction Act.

Meadville Medical Center and Titusville Area Hospital respectfully request that CMS consider excluding safety net providers such as sole community hospitals and critical access hospitals from the proposed negotiated manufacturer price methodology.

Our health system, which consists of a sole community hospital, a critical access hospital, and several rural health clinics is in an under-served area in northwest Pennsylvania. We are the only remaining independent health system in our area, with most smaller hospitals succumbing to acquisition by larger health systems. Our health system provides much needed behavioral health, endocrinology, and medical and radiation oncology in addition to many other services to patients within our community. Prior to providing an oncology service, our community members had to travel hundreds of miles to a larger facility to receive their treatments. This was difficult for patients especially after receiving chemotherapy treatments and unfortunately there is a large volume of cancer patients in our area.

In addition, pharmacy manufacturer mandates within the 340B program, the PHE, increased nursing staff expense, labor shortages, payer reimbursement policy changes, increases in denials, etc. have caused significant financial and operational hurdles to overcome.

The Inflation Reduction Act, as currently written, will also have unfavorable ramifications to our health system in several ways. First, regarding 340B, our savings from contract pharmacies is based upon the contract pharmacies' reimbursement. The reimbursement for the selected drugs for Medicare patients will cause a decrease in our 340B savings. Second, when the Act expands to Part B in 2026, not only will we see a decrease in our Medicare reimbursement for the selected drugs, our commercial reimbursement will also decrease for these same drugs because most of our commercial reimbursement contracts are based upon a mark up above Medicare rates.

For these reasons and more, we respectfully request that CMS exclude SCHs and CAHs from the MFP methodology.

Thank you for your consideration.

Respectfully,
Ellie Amory



266 West 37th Street, 3rd Floor
New York, NY 10018
212.869.3850/Fax: 212.869.3532

April 13, 2023

VIA ELECTRONIC SUBMISSION

The Honorable Meena Seshamani, M.D., Ph.D.
Director, Center for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Dr. Seshamani,

The Medicare Rights Center (Medicare Rights) appreciates this opportunity to comment on initial guidance from the Centers for Medicare & Medicaid Services (CMS) regarding the **Medicare Drug Price Negotiation Program** (Negotiation Program). Medicare Rights is a national, nonprofit organization that works to ensure access to affordable and equitable health care for older adults and people with disabilities through counseling and advocacy, educational programs, and public policy initiatives. Each year, Medicare Rights provides services and resources to over three million people with Medicare, family caregivers, and professionals, including through our national helpline.

General Comments

Based on this experience, we know people with Medicare are uniquely impacted by high and rising drug prices. This is partly due to utilization and health status. Over two-thirds of Medicare beneficiaries have multiple chronic conditions¹ and Part D enrollees take 4 to 5 prescriptions per month, on average.² Many live on fixed or limited incomes that cannot keep pace with rapidly escalating drug prices. Half of all beneficiaries, nearly 30 million people, live on \$29,650 or less per year, and one quarter have less

¹ Centers for Medicare & Medicaid Services, "Multiple Chronic Conditions" https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Chronic-Conditions/MCC_Main.

² Leigh Purvis, *et al.*, "Rx Price Watch Report: Trends in Retail Prices of Specialty Prescription Drugs Widely Used by Older Americans, 2006 to 2020" AARP Public Policy Institute (September 28, 2021) <http://www.aarp.org/rxpricewatch>.

than \$8,500 in savings.³ Health care costs comprise a large and disproportionate share of beneficiaries' limited budgets: nearly 30% of Medicare households spend 20% or more of their income on health care, compared to only 6% of non-Medicare households.⁴ Out-of-pocket costs for prescription drugs represent a significant share of this amount, accounting for nearly one out of every five beneficiary health care dollars.⁵ Most people with Medicare cannot afford to pay more for care.

Callers to our national helpline regularly report struggling to afford the prescription medications they need to maintain their health and well-being. And they are not alone. In 2021, over 5 million people with Medicare are estimated to have had difficulty paying for their prescriptions, with Black and Latino beneficiaries being disproportionately affected.⁶ That same year, nearly twenty percent of older adults said they had not filled a prescription in the past two years, most due to affordability concerns.⁷ Yet, drug costs continue to climb—price hikes on brand name medications have exceeded the rate of inflation every year since at least 2006.⁸

The Inflation Reduction Act's (IRA) Negotiation Program could provide much-needed relief, lowering prices, increasing medication adherence, and improving outcomes. We commend CMS for this timely initial guidance, and respectfully offer the following comments on bolstering **Affordability, Accuracy, and Transparency**.

Affordability

We ask CMS to revisit plans to base aspects of the initial maximum fair price on Part D net prices for therapeutic alternatives. Evidence consistently shows these prices are inflated; Medicare Part D pays significantly higher drug prices than other health programs in the U.S. and abroad.⁹ According to the Government Accountability Office, Part D net prices were up to four times higher than comparable countries in 2020.¹⁰ Using these flawed payments as anchor points would bake overpayment into the

³ Wyatt Koma, *et al.*, "Medicare Beneficiaries' Financial Security Before the Coronavirus Pandemic" Kaiser Family Foundation (April 24, 2020) <https://www.kff.org/medicare/issue-brief/medicare-beneficiaries-financial-security-before-the-coronavirus-pandemic/>.

⁴ Juliette Cubanski, *et al.*, "The Financial Burden on Health Care Spending: Larger for Medicare Households than for Non-Medicare Households" Kaiser Family Foundation (March 1, 2018) <https://www.kff.org/medicare/issue-brief/the-financial-burden-of-health-care-spending-larger-for-medicare-households-than-for-non-medicare-households/>.

⁵ Kaiser Family Foundation, "10 Essential Facts about Medicare and Prescription Drug Spending" (January 29, 2019) <https://www.kff.org/infographic/10-essential-facts-about-medicare-and-prescription-drug-spending/>.

⁶ U.S. Department of Health and Human Services, Assistant Secretary for Planning and Evaluation "Prescription Drug Affordability among Medicare Beneficiaries" (January 19, 2022), <https://aspe.hhs.gov/reports/medicare-prescription-drugs>.

⁷ AARP, "Consumer Views on Prescription Drugs Survey" (July 2021) https://www.aarp.org/content/dam/aarp/research/surveys_statistics/health/2021/drug-prices-older-americans-concerns.doi.10.26419-2Fres.00476.001.pdf.

⁸ Leigh Purvis, *et al.*, "Rx Price Watch Report: Trends in Retail Prices of Specialty Prescription Drugs Widely Used by Older Americans, 2006 to 2020" AARP Public Policy Institute (September 28, 2021) <http://www.aarp.org/rxpricewatch>.

⁹ See, e.g., Government Accountability Office, "Prescription Drugs: Department of Veterans Affairs Paid About Half as Much as Medicare Part D for Selected Drugs in 2017" (January 14, 2021) <https://www.gao.gov/products/gao-21-111#:~:text=What%20GAO%20Found,in%20the%20Part%20D%20program>; Mulcahy, *et al.*, "International Prescription Drug Price Comparisons" (2021) https://www.rand.org/pubs/research_reports/RR2956.html; Government Accountability Office, "Prescription Drugs: U.S. Prices for Selected Brand Drugs Were Higher on Average than Prices in Australia, Canada, and France" (April 28, 2021) <https://www.gao.gov/products/gao-21-282>.

¹⁰ Government Accountability Office, "Prescription Drugs: U.S. Prices for Selected Brand Drugs Were Higher on Average than Prices in Australia, Canada, and France" (April 28, 2021) <https://www.gao.gov/products/gao-21-282>.

Negotiation Program and undermine the IRA’s ability to achieve meaningful cost savings for current and future beneficiaries.

Instead, we urge CMS to use a cost-effectiveness approach. We recommend establishing targets for a preliminary price range which could then be adjusted based on relevant factors (such as comparative effectiveness research, the prices of therapeutic alternatives, and other manufacturer-specific data) to arrive at a maximum fair price.

Accuracy

CMS notes that in calculating maximum fair prices, the agency will rely on cost and projection data from drug manufacturers. However, CMS does not discuss plans to independently verify these “assumptions and calculations.” This is problematic. As for-profit companies, drug manufacturers will necessarily be incentivized to create a financially favorable environment. Past industry behavior even provides a template. An OIG review of the Medicaid Drug Rebate Program found manufacturer reports misclassified drugs in ways that benefitted their bottom line, but cost Medicaid over one billion dollars.¹¹

Not all drug companies are bad actors and not all profit-seeking behaviors are deliberate. Guardrails are therefore needed to prevent similarly intentional, as well as inadvertent, cost-shifting and rebate losses in Medicare. We strongly urge CMS to rely on independent information, to carefully review all collected data, and to conduct both random and for-cause audits .

Transparency

We recognize the IRA affords CMS discretion in releasing information and feedback requests. We applaud CMS for soliciting these and other public comments and encourage the agency to maximize transparency throughout the implementation process.

Accordingly, we ask CMS to reconsider restricting access to information regarding the maximum fair price methodology. While we understand the desire to avoid revealing details the drug manufacturers consider to be proprietary, they must not be allowed to use this as a shield; our health system needs more transparency and accountability, not less.

Program integrity and implementation obligations demand CMS release as much data as possible. This includes the factors and value frameworks used to determine a maximum fair price, as well as any information received from drug manufacturers. These details are necessary to advance general and payer understanding of the cost and value of the negotiated drugs. Without it, other insurers will be unable to effectively negotiate—limiting downward pricing pressure and the IRA’s impact, potentially derailing opportunities for further reform.

¹¹ Department of Health and Human Services, Office of Inspector General “Potential Misclassifications Reported by Drug Manufacturers May Have Led to \$1 Billion in Lost Medicaid Rebates” (December 2017) <https://oig.hhs.gov/oei/reports/oei-03-17-00100.pdf>.

Publicizing this information would also serve as a mechanism for oversight and help encourage accurate, complete manufacturer reporting. The IRA's landmark Negotiation Program must not be shrouded in secrecy.

Conclusion

Thank you again for the opportunity to provide comment. For additional information, please contact me at LCopeland@medicarerights.org or 202-637-0961 or Julie Carter, Counsel for Federal Policy at JCarter@medicarerights.org or 202-637-0962.

Sincerely,

A handwritten signature in cursive script that reads "Lindsey Copeland".

Lindsey Copeland
Director of Federal Policy
Medicare Rights Center



April 14, 2023

Dr. Meena Seshamani
Deputy Administrator and Director, Center for Medicare
Centers for Medicare & Medicaid Services
US Department of Health and Human Services
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Dr. Seshamani,

FasterCures thanks the leadership of the Centers for Medicare & Medicaid Services (CMS) for the opportunity to comment on the initial guidance for the implementation of sections 11001 and 11002 of the Inflation Reduction Act (IRA) (P.L. 117-169) which established the Medicare Drug Price Negotiation Program (Negotiation Program). The Negotiation program represents a landmark opportunity to reduce the financial burden of drug costs on Medicare beneficiaries while also curbing CMS' spending on Part D and Part B drugs. However, the tight timeline specified in the IRA for implementation could pose problems for how well CMS is able to obtain feedback from stakeholders, especially patient communities that will be directly impacted by these changes. We offer some considerations to CMS in this letter to ensure that the perspective of patients is effectively incorporated into the Negotiation Program and to guarantee that the overarching goals of reducing the financial burden and improving access to much-needed medical products for patients are met.

FasterCures, a center of the Milken Institute, is driven by a singular goal: to save lives by speeding scientific advancements to all patients. With an independent voice, FasterCures is working to build a system that is effective, efficient, and driven by a clear vision: collaborating with our partners to build a patient-centric system where science is accelerated, unnecessary barriers are overcome, and lifesaving and life-enhancing treatments get to those who need them as rapidly and as safely as possible.

Patient communities have a critical perspective to consider in the medical product development and coverage process. Decision-makers across the continuum, including regulators, are leading the charge in engaging patients, and we consider the Negotiation Program as an important opportunity for CMS to put in place systems that adequately weigh and incorporate factors that matter to patients as part of its decision-making. The initial guidance released by CMS for the Negotiation Program indicates when CMS will consider patient-reported data and insights. We urge CMS to provide details around its approach for doing so in the ways discussed below.

Ensure sufficient timing and process for patient input. The current timeline for stakeholders to provide input to CMS for the Negotiation Program might be prohibitive for patient organizations, most of whom are already dealing with capacity constraints and are balancing competing demands on their limited time and resources. As such, we are concerned that these organizations may not have sufficient time to gather meaningful data to inform CMS' processes. A key example of one such restrictive timeline is the 30-day comment period that is offered for stakeholders to respond to the list of drugs selected by CMS for negotiations. Recognizing that the initial guidance document applies to drugs selected for the initial year 2026 of the Negotiation Program, we urge CMS to establish an ongoing process for soliciting and receiving patient feedback. We applaud CMS's efforts to diligently solicit input from different stakeholder groups all along the way. CMS can formalize that process specifically for patient groups. Such a process

could provide valuable patient insight that can be used to refine guidance for the subsequent years of the Negotiation Program as well as flagging unintended consequences that could be detrimental to patients and counter to the program's intended goals. The FDA offers a roadmap for how it has instituted systems and programs for ongoing patient input over time. Starting as early as 1998 with the establishment of the Office of AIDS Coordination, through the launch of the Patient Focused Drug Development program in 2012, and continuing to the present day, the FDA has multiple opportunities for patients and patient communities to engage with FDA staff and provide input. We urge CMS to consider a formal system for ongoing input from patient communities as part of the Negotiation Program. This may include dedicated staff and a channel for the patient community to engage with CMS staff.

Provide clarity about use of patient experience data. We are pleased with CMS's incorporation of patient experience data into the Negotiation Program process. Patients offer valuable insights into outcomes that matter to them, tolerability and side effects of products, and their perspective on the risks and benefits associated with medical products. As such, they can inform the identification of therapeutic alternatives for selected products for the Negotiation Program. While Section 50.2 of the guidance calls for broad input of stakeholders, including Medicare beneficiaries in the identification of alternative therapies and Section 60.3.3 mentions that CMS will use patient experience data in considering the clinical benefits of selected drugs and their therapeutic alternatives, the guidance currently lacks important details. Specifically, the guidance does not include details on the kinds of data, e.g., registry, natural history studies, patient preferred outcomes and others, that CMS will find beneficial, and how much patient experience data will weigh into its decision regarding revising its offer price for selected products. This kind of detail will help patient communities streamline their efforts as they gather data to share with CMS. We encourage CMS to provide more details to this effect in the final guidance and to prioritize patient input as a substantial part of its consideration.

The use of patient experience data as part of the Negotiation Program also offers an opportunity for CMS and FDA to be aligned in their evidentiary requirements, especially as it pertains to the collection and use of patient input as part of regulatory and coverage decisions. While this particular point may have longer-term implications, we believe that this kind of alignment could galvanize the move toward more patient-centricity in medical product research, development, and access. In the last few years, product manufacturers have recognized the importance of engaging patients from the onset of the drug research and development process. With FDA encouragement, manufacturers are already actively gathering patient input that they are considering in the application process. Some medical product manufacturers have not accepted patient engagement as a core function of their product development lifecycle and may struggle to capture the value in engaging patients in a way that aligns with their organizational priorities. By providing details on the types of patient input that it will be considering as part of its review in the drug negotiation process, CMS will be helping manufactures preempt, align, and address the needs of the regulatory and drug negotiation process from the onset of drug research and development. This could also result in efficiencies for patient organizations that have to respond to multiple demands from medical product manufacturers, often for the same information.

Thank you for the opportunity to provide comments on this important program. We look forward to the updated guidance with stakeholder feedback and welcome any opportunities to support CMS in your efforts as you implement the Negotiation Program.

Sincerely,



Esther Krofah
Executive Vice President of Health
Executive Director, FasterCures and Center for Public Health
Milken Institute

April 14th, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201_
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Mineralys Therapeutics, Inc. appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

Mineralys Therapeutics, Inc. is a clinical-stage biopharmaceutical company focused on developing medicines to target diseases driven by abnormally elevated aldosterone with our novel aldosterone synthase inhibitor, lorundrostat. Our mission is to bring lorundrostat to the market to address the significant unmet needs in hypertension, chronic kidney disease, heart failure and other disease conditions driven by abnormal aldosterone elevation. Uncontrolled blood pressure is the leading cause of heart disease, stroke and chronic kidney disease, all of which represent significant economic burden to the healthcare system and are also leading causes of death or disability in the United States.

The provisions of the IRA materially impact Mineralys and our plans to develop lorundrostat, a small molecule. The Hatch-Waxman act provided a clear path for efficiently introducing generic medicines into the U.S. healthcare system. As a former employee of Teva, the world's leading generic medicine manufacturer, I saw the symbiotic relationship of brands, bringing innovative solutions to healthcare, and generics, bringing economic benefits. This developed into an efficient system with small molecules that has not been as easily translated with large molecules such as antibodies. The disparity of treatment in the IRA with small molecules relative to large molecules, completely neglects this efficiency and penalizes small molecule developers. The IRA further hinders drug development with small molecules such as lorundrostat, that may provide significant medical value beyond the initial indication.

Applying the 13 year rule to small molecules, the same as large molecules, enables companies like Mineralys to commit additional capital to fully elucidate the value of their development candidate with the opportunity to achieve a return on that broader investment. These broader innovations stand to benefit patients in the near-term and longer term once generics are available. Our development candidate, lorundrostat, is an excellent case study. Our initial indication is hypertension, but there is a high probability of benefit with lorundrostat in chronic kidney disease and heart failure given the role of aldosterone in these diseases. Unfortunately, the shift to a nine-year period would

force companies like Mineralys to abandon further investigation of their compound as the economics do not support this effort. This would represent a significant loss to the healthcare system and further constrain innovation.

While I recognize that CMS is not accepting comments to Section 30, I am compelled to provide my recommendations in the hopes of impacting the ultimate outcome of this new law.

- I. Section 30.1: Change the timing for the NDA-path negotiations from 9 years to the same 13 year period as for BLA-path drugs. While 13 years is less than the typical 14 years of marketing exclusivity afforded by patent protection, investment can recalibrate slightly to one less year with very slightly higher launch prices so as to keep drug R&D investible. The harms from IRA's treatment of orphan drugs could be mostly alleviated by creating small- and large-molecule parity for negotiation at 13 years. CMS should look to only active orphan drug designations for the purposes of determining eligibility for the orphan drug exclusion (not including withdrawn orphan drug designations).
- II. Section 50.2: To the extent that CMS wants to appreciate the value that a medicine brings to society before it decides how aggressively to lower its price (particularly in the case of NDA-path drugs that experience negotiation far sooner than would have gone generic), CMS should broadly account for a medicine's value elements, using a dynamic stacked cohort model that accounts for value to patients, to caregivers, and to the rest of the population whose risk is reduced by having the drug (i.e., if it's going to do CEA, do generalized CEA, not conventional over-simplified CEA). CMS should consider key product attributes like efficacy, safety, and ease-of-use in determining relevant "therapeutic alternatives" (the basis for CMS' opening bid).
- III. Section 90.4: The IRA threatens to make generic business models unsustainable for drugs that treat Medicare populations. One might think this doesn't matter because price reduction will be achieved via negotiation. However, because generic competition often drives costs down not only by eroding the gross margins of the original drug but also spurring manufacturing improvements that lower cost of goods, the IRA threatens to leave society paying more for old drugs in the long run by deterring generic competition. This could increase overall costs across market segments (Medicare and commercial payers).
- IV. Section 40.2.2: CMS's process for determining value and cost-effectiveness should be transparent (vs. gag order and document destruction that they propose today). It should be able to defend what it considers to be a "fair price." Furthermore, this prohibition violates company First Amendment rights. Companies subject to the negotiation process need to be able to disclose to their boards and their investors what occurred in the negotiation process.

* * * * *

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact Jon Congleton, CEO, by telephone at (816) 585-7739 or by e-mail at jcongleton@mineralystx.com if you have any questions regarding our comments.

Best regards,

DocuSigned by:

Jon Congleton

EE54FE0D28A4436...

Jon Congleton

CEO

Mineralys Therapeutics, Inc.

Section 30.1.1 of the initial guidance outlines CMS’s interpretation of the Orphan Drug Exclusion (ODE) from the broader qualifying single-source drug definition. Our understanding of the provision enacted under Section 1192(e)(3)(A) of the Social Security Act, as amended by the Inflation Reduction Act (IRA), was that orphan drugs would qualify for the ODE so long as they had received FDA approval for just one rare disease or condition, even if approved for multiple indications across a single disease (i.e. multiple age groups for a rare blood disorder). We would contend that this interpretation comports with the **original public understanding** of the legislation, as enacted, in keeping with core principles of statutory interpretation. For example:

- In an [August 10, 2022 article in *Health Affairs*](#) explaining the prescription drug provisions in the IRA, scholar Rachel Sachs described the ODE in a manner consistent with our understanding, noting that “[c]ertain products, **such as drugs whose only approved indication(s) are for a single rare disease or condition**, or plasma-derived products, are categorically excluded from negotiation” (**emphasis mine**).
- An [April 7, 2022 report from the Institute for Clinical and Economic Review \(ICER\)](#) described an essentially identical ODE provision from an earlier iteration of the legislation as “exclud[ing] drugs with only one orphan indication from Medicare price negotiation.”
- A [January 27, 2023 *JAMA Health Forum*](#) study simulating drug price negotiation under the law asserts that eligible drugs “cannot be approved to treat a single rare condition (as designated under the Orphan Drug Act),” referencing the ODE provisions.
- A [January 24, 2023 Kaiser Family Foundation issue brief](#) outlining the law’s drug pricing provision specifies that the ODE encompasses “[d]rugs with an orphan designation as their only FDA-approved indication.”
- A [February 27, 2023 *Avalere* piece](#) discussing orphan drugs echoes this same interpretation, noting that the ODE “applies only to those orphan drugs with an approved indication (or indications) for a single rare disease or condition.”
- An [October 11, 2022 summary from Akin Gump](#) notes, “Among those excluded [from negotiation eligibility] are products with only one Orphan Drug indication.”
- A [March 1, 2023 piece](#) from the Council on Affordable Health Coverage describes the ODE using this same interpretation, noting the disincentive the legislation triggers for receiving additional orphan indication approvals (a concern we share, but one that we acknowledge would require a legislative remedy).
- An [August 18, 2022 summary](#) from DLA Piper characterizes the ODE as applying to “[o]rphan drugs that treat only one rare disease.”

As illustrated by these and other examples, the public has, since even before final enactment, understood the ODE under the IRA to apply on the basis of **approved indications**, irrespective of designations for unapproved or not-yet approved indications. We share this common understanding. Insofar as the language in the law contains ambiguity, we encourage CMS, consistent with basic principles of statutory interpretation, to resolve any ambiguous phrasing in favor of the standard reading of the provision's purpose, intent, and scope, as outlined by the experts, scholars, legal minds, and stakeholders referenced above, among numerous others.

This general public understanding also aligns with a **contextual interpretation** of the scope of the ODE, lending additional credence to our reading of the language in question. Notably, for instance:

- The clear aim of the provision in question is to preserve incentives for orphan drug development, consistent with the Orphan Drug Act policies and other incentives provided by Congress (on a bipartisan basis) to encourage and reward research and development regarding rare disease treatments (an otherwise challenging and fraught enterprise—and still a high-risk endeavor, given the erosion of many of these statutory and regulatory incentives), without enabling manufacturers to a) bypass negotiation eligibility by pursuing orphan indications for high-profit products (i.e. a rare cancer indication for a blockbuster, multipurpose cancer drug) or b) effectively 'stack' orphan indications in order to avert negotiation eligibility while capturing a high patient volume (with high prices) across a range of rare conditions. Regardless of the merits or deficiencies of this policy approach, the scope of the ODE clearly hinges on an effort to balance orphan drug development incentives with potential abuses. Lending support to this interpretation, Anna Kaltenboeck, my former counterpart and the lead Senate Democrat staffer on the legislation (as enacted) has described this dynamic and perception in public commentary, [noting](#), in one rare disease-focused discussion: "The question is how to create a system of incentives where you do encourage these smaller companies and continue to protect them without also keeping monopolistic and anticompetitive behavior and protecting that — you have this tension always in that system."
- In other words, without *approval*, under the drafters' view of pricing dynamics, a *designation* holds no potential for pricing abuse or "gaming" of the negotiation system, since approval provides the primary avenue for generating patient volume, and thus revenue. For off-label uses, existing statute presents substantial guardrails that make patient uptake a challenge (and potential liability) from a coverage and regulatory

standpoint. In context, the provision here, even if drafted with some degree of ambiguity, clearly aims to prevent drugs **approved** to treat multiple indications from sidestepping negotiation indefinitely.

- From a CMS coverage and payment standpoint, a designation has virtually no meaning unless attached to an FDA-approved indication. Interpreting the ODE as we have aligns, for instance, with other CMS-specific treatment of orphan drug products. In one illustrative example, under the Competitive Acquisition Program, CMS [specified](#), “Approved CAP vendor may request that CMS allowed it to supply **single indication orphan drugs** under the CAP.” Interpreting the ODE as excluding orphan drug products with indications for a single rare disease would align with this approach, grounded in CMS agency precedent.
- For CMS to bar ODE eligibility on the basis of multiple **designations**, even if only one such designation has resulted in an **approval**, would represent a substantial anomaly and departure from precedent on the part of CMS, which has no role in the orphan designation process. Orphan designations do not, in and of themselves, trigger **any meaningful action on the part of CMS**, whereas FDA-approved indications generally result in automatic coverage (or, in the case of certain products, a coverage determination process). In interpreting the ODE consistent with the general public understanding, CMS would thus maintain its current scope and statutory (and regulatory/sub-regulatory) roles and responsibilities, lending additional support to this contextual interpretation.
- The ODE refers to a categorical exclusion, and so reading any one piece of the language in isolation could produce an ambiguous or self-contradictory interpretation. “Designation,” when read in the context of the rest of the provision in question, seems designed to stipulate that the exclusion captures only drugs with an FDA-granted orphan designation.

As CMS finalizes the guidance for the Drug Price Negotiation Program, we encourage the agency to resolve this apparent ambiguity by exercising its authority to interpret the ODE as applying only to orphan drugs with approved indications for a single rare disease or condition, and we urge CMS to consider avenues to interpret “rare disease or condition” with sufficient breadth to capture sub-conditions under an adequately sizable ‘disease or condition’ category so as to preserve incentives for drug development across sub-conditions, where a single product can have significant productive capacity. These steps would align with CMS’s stated goal “to best support orphan drug development.” Interpreting the ODE as applying only to drugs with a single orphan **designation**, regardless of FDA approval(s), would conflict with the general public understanding of the ODE, as well as a contextual reading of the provision in question. Such a narrow interpretation would conflict with basic principles of statutory interpretation, stifle rare disease drug development, and penalize medication developers for pursuing

clinical programs for indications that may well result in failure, limiting the potential of discovery and development initiatives.

We also encourage CMS to work with Congress to remedy the existing ODE's problematic scope, which discourages manufacturers from pursuing new uses of existing orphan drugs, as approved indications for multiple rare diseases would improve the lives of patients. Under the current framework, investors and innovators may forego the research and development needed to identify and seek approval for these indications, recognizing that doing so would risk exposing them to the negotiation program's mandatory and escalating price reductions.

Conor Sheehey
Senior Health Policy Advisor
U.S. Senate Committee on Finance



April 14th 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Meena Seshamani, M.D., Ph.D.,
Deputy Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244

Re: Medicare Drug Prescription Pricing Negotiation Program

Dear Ms. Brooks-LaSure and Dr. Seshamani,

In service of the neuromuscular disease (NMD) patient community, the Muscular Dystrophy Association (MDA) thanks the Center for Medicare and Medicaid Services (CMS) for the guidance released on March 15th 2023, about the Medicare Prescription Drug Negotiation Program (The Program) as required by the *Inflation Reduction Act of 2022* (IRA).

MDA is the nation's leading nonprofit organization dedicated to empowering the lives of individuals living with neuromuscular diseases through innovations in science and innovations in care. MDA fulfills its mission by funding biomedical research, providing access to expert clinical care and support through its national MDA Care Center Network, and championing public policies and programs that benefit those we serve. Since its inception, MDA has invested more than \$1 billion in research grants to accelerate treatments and cures for neuromuscular disorders, making MDA the largest source of neuromuscular disease research funding in the U.S. outside of the federal government.

Background:

The Maximum Fair Price (MFP) provisions of the IRA provide the CMS with the authority to negotiate with drug companies for certain medications reducing drug prices for Medicare beneficiaries. CMS's guidance recognizes that the MFP provisions of the law also include provisions to protect patients and support patient centered action. CMS has the opportunity to continue advancing this crucial goal throughout the implementation of The Program.

Given the relatively few rare diseases that have an FDA approved treatment, continued research and innovation will remain vital. Therefore, as CMS continues to implement this provision of the IRA, we ask that you continue to further consider the unique perspective brought and challenges

faced by those with rare neuromuscular diseases. To best support these communities, we offer the following recommendations:

Patient Access:

MDA emphasizes the need for beneficiary protections in access to care while CMS undertakes the new drug price negotiation process. We are optimistic that the provisions of the IRA which require products within the Medicare Part D, and eventually Part B, plans to be included in negotiations have the potential to reduce out-of-pocket expenses for Medicare beneficiaries. However, with these negotiations come various concerns relating to patient access. We encourage CMS to protect beneficiary access to eligible drugs to ensure that there are as few barriers to access to them as possible. This protection should include both negotiated drugs, and ensuring unintended deleterious effects toward access to non-negotiated drugs do not occur.

This oversight should include monitoring changes to formularies and utilizing the highest practicable specialty tier to reduce out-of-pocket costs. Additionally, we would ask that CMS eliminate denials or delays of treatment for the rare neuromuscular disease community. Eliminating these denials is particularly important for those with rare neuromuscular diseases as many of these conditions are progressive. If there is a delay in appropriate care due to utilization management, a patient's disease state could irreversibly progress further. Those with rare diseases and their healthcare providers are best positioned to decide on the best course of treatment. This combined with CMS's determination that the drugs under covered by The Program have been priced fairly should mean that utilization management tools such as step therapy or prior authorization can and should be limited or eliminated by CMS for these products.

Orphan Drug Exemption:

MDA appreciates that the IRA includes a limited exemption for orphan drugs that only treat one rare disease from drug price negotiation. However, we are concerned CMS's current interpretation of this rare disease exemption, which makes products eligible for negotiation if they have been designated for two or more orphan diseases, even if the drug is not actually FDA approved to treat the second orphan disease, will disincentivize drug companies from conducting even the basic research necessary to develop a drug for additional rare diseases. We have already potentially seen this disincentive in real time. Two companies, Eli Lilly¹ and Alnylam², have, if nothing else, both cited concerns with the IRA's consideration of the orphan drug exemption as cause for halting their development. While the IRA may not be the sole reason for their

¹ Gelman, Updated: Eli Lilly blames Biden's IRA for cancer drug discontinuation as the new pharma playbook takes shape. Endpoints News, Nov. 2022. <https://endpts.com/eli-lilly-rolls-snake-eyes-as-it-axes-two-early-stage-drugs-including-a-40m-cancer-therapy-from-fosun/>

² Liu, As Amvuttra makes inroads in ATTR, Alnylam scraps heart disease trial interim analysis, rethinks another rare disorder plan. Fierce Pharma Oct. 2022. <https://www.fiercepharma.com/pharma/amvuttra-makes-inroads-attr-alnylam-scraps-heart-disease-trial-interim-analysis-rethinks>

hesitation, it is, at a minimum, noteworthy. We urge CMS to clarify that obtaining additional designations for a small molecule or biologic will not make a drug negotiation eligible until the drug has been approved by FDA to treat a second disease or condition.

Excluding the utilization of Quality-Adjusted Life-Years (QALYs) in the negotiation process:

MDA applauds the IRA's prohibition of CMS's use of QALYs in The Program. QALYs rely on an inherently ableist and utilitarian concept of quality of life and assumes outcomes for able-bodied patients in perfect health. Such ableist assumptions about what constitutes a "good" quality of life in determining treatment effectiveness for patients with disabilities fail to consider other factors such as emotional wellbeing, the personal wishes, and aspirations of the patient, the will to live, the personal beliefs of the patient among others. As such, we are grateful for CMS's adherence to the IRA in their implementation and their willingness to further underline their exclusion of these metrics in the proposed guidance. However, CMS's proposal may exclude other helpful metrics in their establishing the value of a drug which will be crucial in the negotiation process (see below). Therefore, we ask that CMS offer additional information for how CMS will consider its approach to gathering information as to the effectiveness of therapies.

Comparative effectiveness:

MDA supports CMS's considerations of differing methods to evaluate the value of a prescription drug for patients. Among the different methods for valuation we ask that CMS consider, as discussed above, the value of slowing or halting disease progression. Given the relatively few options available to treat many neuromuscular diseases it is important to note that many drugs in this space may not share the exact same indications or be used by the same patient populations. Similarly, some drugs in this space may be the only therapy in a specific class to treat a condition while also falling outside of orphan drug exclusions. We urge CMS to approach these considerations holistically rather than myopically focusing on the lower cost drug. Doing so may disincentivize manufacturers from investing in further innovations in these disease areas.

MDA does not singularly support any one metric. Specifically for gene and cell-based therapies, one potentially applicable value assessment method is one such as those for "Single or Short-Term Transformative Therapies" (SSTs). SSTs "are defined as therapies that are delivered through a single intervention or a short-term course of treatment that demonstrate a significant potential for substantial and sustained health benefits extending throughout patients' lifetimes."³ Regarding SSTs, it is important to note from the outset that, first, SSTs are mostly only used for gene therapies and cell-based therapies, and therefore are likely inapplicable to other classifications. Second, The Institute for Clinical and Economic Review (ICER) uses QALYs in

³ Institute for Clinical and Economic Review, Value Assessment Methods Such as Those for "Single or Short-Term Transformative Therapies" (SSTs), Aug. 2019. https://icer.org/wp-content/uploads/2020/10/ICER_SST_ProposedAdaptations_080619-2.pdf

its consideration of SSTs. As noted above, MDA roundly rejects the use of QALYs and we would only support the use of a method such as SSTs if QALYs were removed from consideration. With this background, however, given the rarity of the conditions SSTs consider and particularly the expense of these medications, the metrics by which these medications are considered may prove useful to CMS's current considerations. As MDA noted,⁴ in recent comments to ICER there are areas in assessing the value of neuromuscular disease therapies that warrant better consideration methods.

Particularly, we rejected ICER's concerns about "added dimensions of value." One such value to highlight the value of hope. ICER initially highlighted the importance of choice with an eye toward a risk benefit analysis with choices between therapies. We, however, see the value of hope as the potential for a more healthy and happy life in the future than was previously expected. SSTs offer patients the possibility of substantially healthier lives many years into the future, and with this brings the hope of attending college, getting married, and other important life experiences. In addition, we raised other concerns with ICER's perspective on scientific spillover which relates somewhat to our comparative effectiveness discussion above and flexible cost-valuation thresholds (though we reject the use of QALYs), and patient-focused expectations (see below). All of these metrics could prove useful for CMS's future consideration for comparative effectiveness.

We further discourage CMS from relying on equal-value Life Years Gained (evLYGs) as an alternative metric to QALYs. While evLYGs avoid the most egregiously discriminatory aspects of QALYs, they are an imperfect measure that inherently devalues the health and wellbeing benefits an intervention may bring the beneficiary by disregarding quality-of-life improvements entirely.

Evaluation approaches exist that do not discriminate against those with disabilities while also capturing quality-of-life benefits. For example, one such method similar to QALYs are Health Years Total (HYT). HYT is a valuation method which modify QALYs by separating evaluations of life expectancy and quality of life improvement whereas QALYs consider these concepts as a single consideration. Additionally, HYTs do not consider utility values in its evaluation of life expectancy. However, HYTs do, unfortunately, still consider utility to values to discount quality of life improvement.⁵ While not a perfect solution, HYTs do still represent an improvement compared to using QALYs. One method which eschews QALY's methodology altogether is The Efficiency Frontier (EF). EF takes into consideration condition-specific measures. EF benchmarks the price and benefit of the new therapy being considered against the value provided

⁴ See generally, [MDA Comments on ICER's SST Adaptations](#)

⁵ Gallegos, *Alternatives to QALY-Based Cost-Effectiveness Analysis for Determining the Value of Prescription Drugs and Other Health Interventions*, National Council on Disability, 7, Nov. 2022. https://ncd.gov/sites/default/files/NCD_Alternatives_to_the_QALY_508.pdf See also, Disability Rights Education & Defense Fund, *ICER Analysis Based on the QALY Violate Disability Nondiscrimination Law*, 27, Sep. 2021. <https://dredf.org/wp-content/uploads/2021/09/ICER-Analyses-Based-on-the-QALY-Violate-Disability-Nondiscrimination-Law-9-17-2021.pdf> [hereinafter referred to as DREDF]

by existing drugs to calculate cost per outcome unity which then informs the recommendation for the cost of the new drug.⁶ In addition to these two methods there are methodologies such as Generalized Risk-Adjusted Cost-Effectiveness (GRACE) and Burden Augmented by Deadliness and Impact (BADI) among *many* others.⁷ To reiterate, MDA does not recommend at this time any one non-discriminatory valuation technique over another, and only seeks to posit options outside of the use of QALYs for CMS's consideration.

Patient Input for Future Improvement:

The implementation of The Program will be a long and complex one and we are heartened that CMS has shown themselves to be open to feedback. We hope that this attitude will continue. We ask that CMS will monitor the program to ensure that it has the intended effects of increasing access to affordable medications, and again ensuring that lower out of pocket costs are, in fact, realized, and that barriers to access are minimized if not removed entirely.

To that end, we would suggest that CMS implement any of several metrics to continue listening to the voices of those with rare neuromuscular diseases. CMS should continue to utilize patient experience data to ensure effective services are delivered. To best utilize this data, CMS should make use of Requests for Information and listening sessions to ensure the collection of representative data. These processes should allow for as long a timeline as possible and should also streamline and simplify the process for submitting data and information to ensure stakeholders have adequate time to supply information. Similarly, granular summaries of the data and assumptions on which each negotiation was based should be made available to the public.

Finally, as is currently stated in the guidance by CMS the dispute resolution and compliance process under section 1145 of the IRA asks for evidence submitted by the manufacturers and holds that the negotiation and compliance processes will occur between manufacturers and CMS. We ask that CMS consider the voices of neuromuscular disease patients and other stakeholders should either be included in, or at a minimum made aware of, the metrics used in these negotiation and compliance processes. This will not only allow CMS to keep abreast of the voice of the neuromuscular disease community but will also allow the community to better understand the methods by which CMS makes its decisions both with regard to enforcing the requirements of The Program as well the factors they consider in the negotiation process. This information will allow the neuromuscular disease community to better communicate with CMS to improve the process going forward.

Conclusion:

MDA is committed to ensuring that individuals with rare neuromuscular diseases have access to FDA approved therapies to promote safe and healthy lives. We encourage CMS to heed the above feedback as they consider the implementation of The Program.

⁶ *Id.*, at 9. See also, DREDF *Supra* note 5 at *Id.*

⁷ *Id.* at 10-11. See also, DRDEF *Supra* note 5 at *Id.*

We appreciate this opportunity to provide comment on CMS's guidance. For questions regarding MDA or the above comments, please contact me at 336-409-4000 or jcartner@mdausa.org.

Sincerely,

A handwritten signature in cursive script that reads "Joel Cartner".

Joel Cartner, Esq.
Director, Access Policy
Muscular Dystrophy Association

Narrow River Management, LP
River 2 Renal Corp.
River 3 Renal Corp.
7550 Purple Sage
Park City, UT 84098

April 8, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Narrow River Management, on behalf of River 2 and River 2 Renal Corp., appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

Narrow River Management is engaged in the founding and management of companies that develop novel pharmaceutical products for the treatment of serious diseases without adequate current therapies. It has recently founded two companies, River 2 and River 3 Renal Corp., each of which is developing drugs for Orphan indications in the field of kidney disease. Since these companies are developing a peptide and a small molecule, respectively, the implementation of the instant legislation will have a deleterious effect on the companies' prospects going forward.

River 2 Renal Corp. is developing a peptide molecule for hepato-renal syndrome, a disease of acute kidney failure secondary to liver cirrhosis. It is a serious condition with mortality of about 50% at 90 days. Currently, there is only one drug approved for this indication and its efficacy and safety make it a last resort for patients and caregivers. Surviving patients will need a liver transplant and possibly a kidney transplant. If our drug works, it could reduce the number of required kidney transplants, in addition to saving lives. This is an Orphan indication and the proposed limitation on one designation could cause us to reconsider developing the drug in this indication. We are also potentially developing the molecule for heart failure. This latter indication could be considered a disease of aging. As a peptide, R2R's molecule could be subject to price negotiation at 9 years, which would significantly limit the period for return on investment. This is the case, notwithstanding the fact that if the drug should work, it will significantly reduce hospitalization time for patients and, consequently, cost of therapy. As this drug is at an early stage of development and we rely on venture capital investment to fund clinical development, this legislation could adversely affect our ability to raise capital.

River 3 Renal Corp. is developing a small molecule pill for two Orphan diseases – Alport Syndrome (AS) and Focal Segmental Glomerulosclerosis (FSGS). AS causes early kidney failure in mostly adolescent

males. FSGS is a multicausal disease of the kidney which can only be cured with a transplant. The goal of these therapies is to delay renal replacement for as long as possible. Each of these is an Orphan disease, but the proposed legislation would allow us a designation for only one disease, creating a complex and confusing proposition that might cause is to develop the drug for only one. There is currently no drug approved in either indication. The drug may also be efficacious in diabetic kidney disease, which could be considered a disease of aging, possibly subjecting this drug to price negotiation at 9 years should it be approved. As this is a drug at an early stage of development and we rely on venture capital investment to fund clinical development, this legislation could adversely affect our ability to raise capital.

As a result of the above and, more importantly, the many similarly situated companies, we believe it would be in the best interests of the country to modify the current legislation in the following fashion:

- I. Section 30.1. Elimination the arbitrary distinction between biologics and other molecules and make the NDA path to price negotiation 13 years.
- II. Section 30.1.1 Allow Orphan designation for multiple indications.

We appreciate your consideration of our comments. Please feel free to contact me by telephone at +1 917 981 8200 or by e-mail at dmadden@narrowrivermgmt.com if you have any questions.

Very truly yours,



Dave Madden

Chief Executive Officer
River 2 Renal Corp.
River 3 Renal Corp.

Principal
Narrow River Management, LP

April 14, 2023

Honorable Chiquita Brooks-LaSure, Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Submitted via email to Centers for Medicare and Medicaid Services to
IRAREbateandNegotiation@cms.hhs.gov

RE: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure,

The National Academy for State Health Policy (NASHP) appreciates this opportunity to submit this letter of support for the Medicare Drug Price Negotiation Program Guidance issued on March 15, 2023.

Summary of Comments

NASHP developed these comments in consultation with state officials. Comments focus specifically on the intersections of the Medicare Drug Price Negotiation Program (Negotiation Program), state Prescription Drug Affordability Boards (PDABs), and state drug price transparency programs. Ideally, states would like to be able to align with the Negotiation Program and to build upon its work. Key areas for doing so discussed further in comments below include the following:

- Maximizing data sharing and transparency while protecting genuinely proprietary manufacturer data;
- Identifying and realizing opportunities for aligning methodologies, for example, methodologies to address multiple dosage forms and strengths for a single drug; and,
- Exploring the proposed pharmacy chargeback system to implement MFPs in the supply chain as a potential model for states implementing upper payment limits (UPLs).



Overview of NASHP

NASHP is a non-partisan forum of state policy makers that works to develop and promote innovative health care policy solutions at the state level. In 2017 NASHP created its Center for Drug Pricing to work with states to develop strategies to address high prescription drug prices and the impact they have on consumers, the overall cost of health care, and state budgets.

Working with states, and through our Center for Drug Pricing, NASHP developed model policy for Prescription Drug Affordability Boards, enabling states to conduct affordability reviews and to establish upper payment limits for drugs within a state when appropriate. We have worked closely with the six states that have enacted PDABs and are moving forward with implementation, convening them for monthly work group calls for the past several years.

Background

Through implementing PDABs, states have already embarked on work similar, though with important differences, to what CMS is taking on through the Medicare Drug Price Negotiation Program. As such, PDAB states are closely watching implementation of the Negotiation Program, both to learn how these federal efforts might help support state efforts, and also to share how state experiences might help inform the Negotiation Program.

More than a dozen states have also enacted drug price transparency programs, many of which require reporting from drug manufacturers, including data similar to what the Centers for Medicare and Medicaid Services (CMS) requires from manufacturers as part of the Negotiation Program.

Beyond PDABs and drug price transparency programs, legislation has been introduced this session that, if enacted, would allow a state to reference Medicare-negotiated Maximum Fair Prices (MFPs). These proposals indicate both support for the Negotiation Program, and an interest in leveraging the MFPs, once available, at the state-level.

Comments

40.2.1 Confidentiality of Proprietary Information (pgs. 28-29)

This section describes measures CMS will take to safeguard confidential information submitted by drug manufacturers as part of drug price negotiations. States understand and respect the need to maintain such confidentiality, however, some of the information collected (*e.g., “research and development costs and recoupment, unit costs of production and distribution, pending patent applications, and market data and revenue and sales volume data to be proprietary”*) could support state PDABs’ work conducting thorough, accurate affordability reviews to set appropriate upper payment limits.

Final guidance including guardrails for sharing relevant data with states under strict parameters for maintaining the confidentiality of that data, could enable state PDABs to leverage Negotiation Program data while also minimizing reporting burdens on drug manufacturers who may have to report similar data to states.

States that require drug manufacturers to report drug pricing data have encountered manufacturers seeking to classify a very broad range of data as confidential or proprietary, including even data that are already clearly in the public domain. Overly broad requests to treat data as confidential can unnecessarily limit transparency and create the time-consuming task of adjudicating confidentiality claims.

Non-confidential information, including that which might be shared in the explanation of an MFP, could also be instructive for PDABs as described in the comment on Section 60.6.1 below. As CMS seeks to strike the appropriate balance in protecting genuinely confidential information, along with achieving transparency by sharing information publicly through the explanations of MFPs, states would be happy to share more on their relevant experience.

50.1 Manufacturer-Specific Data (pg. 35)

Data submitted by primary manufacturer:

- “1. Research and development costs of the Primary Manufacturer for the selected drug and the extent to which the Primary Manufacturer has recouped those costs;*
- 2. Current unit costs of production and distribution of the selected drug, averaged across the Primary Manufacturer and any Secondary Manufacturer(s);*
- 3. Prior Federal financial support for novel therapeutic discovery and development with respect to the selected drug;*
- 4. Data on pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the FD&C Act or section 351(a) of the PHS Act for the selected drug; and*
- 5. Market data and revenue and sales volume data for the selected drug in the United States for the Primary Manufacturer and any Secondary Manufacturer(s) (with the exception of costs related to the acquisition of the selected drug, which would be reported only for the Primary Manufacturer).”*

The data listed above does not include a request for manufacturers to share data on rebates provided to pharmacy benefit managers (PBMs) for specific drugs. State PDABs and drug price transparency programs have identified rebates as essential yet challenging data to obtain. The Negotiation Program may benefit from a requirement for manufacturers to report rebate data at the drug level.

50.2 Evidence About Therapeutic Alternatives for the Selected Drug (pg. 36)

“CMS will not use QALYs or evidence from comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.”

Most PDABs share similar prohibitions on the use of quality-adjusted life years (QALYs) per their statutes. However, states remain committed to the use of robust health economics and outcomes research in implementing PDABs, including research using expressly non-discriminatory measures such as the Equal Value of Life Years Gained.

60.1 Establishment of a Single Proposed MFP for Negotiation Purposes (pg. 38)

“CMS intends to identify a single price for use at each step in the negotiation process...., even for a selected drug with multiple dosage forms and strengths. Once the MFP has been determined, section 1196(a)(2) of the Act direct CMS to establish procedures to compute and apply the MFP across different dosages forms and strengths of a selected drug, as applicable.... CMS intends to base the single price on the cost of the selected drug per 30-day equivalent supply (rather than per unit – such as tablet, capsule, injection – or per volume or weight-based metric), weighted across dosage forms and strengths, as applicable. For example, if the selected drug is available in a tablet form taken daily as well as an injection form taken every other month, CMS would base the single price for the initial offer on the average cost of (1) 30 tablets and (2) one injection divided by 2 (half the cost of one injection), weighted by number of 30-day equivalents for each presentation as reflected in Medicare Part D utilization during the 12-month period ending May 31, 2023.”

This standardization/weighting process has been challenging for PDABs as well as for state drug price transparency programs. Any additional insight and guidance CMS can share that might enable aligning methodologies concerning how best to address multiple dosage forms and strengths for a single drug and how to appropriately weight them would be helpful for states.

60.3.4 Consideration of Manufacturer-Specific Data (pg. 52)

Data that CMS will consider includes *“research and development cost of the manufacturer for the drug and the extent to which the manufacturer has recouped research and development costs.”*

State drug price transparency programs have sought similar data from drug manufacturers due to the important nature of this component of drug pricing, however, reporting has not yielded the type of meaningful, drug-level data that states were hoping for to better understand how research and development investments relate to drug pricing.



60.5 Application of the MFP Across Dosage Forms and Strengths (pg. 58)

“In order to ensure that the MFP is made available to MFP-eligible individuals at the point of sale (and to pharmacies, mail order services, or other dispensers, with respect to such MFP-eligible individuals) ... CMS intends to publish the MFP at the per unit (e.g., tablet) level for each dosage form and strength associated with the selected drug.”

The publication of MFPs at the per unit-level will be instrumental for state PDABs as well as for states that might wish to reference Medicare MFPs in the future. Additionally, PDABs may wish to align with the methodology for conversation across all relevant dosage forms and strengths.

60.6.1 Explanation for the MFP (pg. 60)

This section describes how and when CMS will share explanations for the MFP, including *“factors that had the greatest influence in determining the MFP and other factors, as applicable....CMS intends to make high-level comments on the data submitted to CMS without sharing any proprietary information.”*

The published explanations for MFPs could provide important data for the work of state PDABs and drug price transparency programs. The explanations will be most useful with the highest level of detail possible that CMS can share without revealing genuinely proprietary information. In making determinations about what to consider proprietary, CMS may wish to consult states on the experiences of their drug price transparency programs, in which drug manufacturers have aggressively classified data as proprietary, including even data that are already available publicly.

The guidance requires the explanation for the MFP to be published no later than March 1 of the year prior to the initial price applicability year. If final guidance might consider an earlier publication schedule, these explanations would be most beneficial to states if made available as soon as possible.

90.2 Monitoring of Access to the MFP (pg.65/66)

The chargeback mechanism by which a pharmacy could be made whole for dispensing a drug with an MFP could be instructive for states and create an opportunity for potential alignment for implementation of MFPs through the supply chain with state implementation of upper payment limits set by PDABs. States will seek to learn from the experience of CMS and stakeholders implementing MFPs and seek to apply that knowledge for state UPLs as appropriate.

NASHP appreciates this opportunity to comment on the Medicare Drug Price Negotiation Program and commends the Administration and HHS for taking this important step towards



lowering drug costs. We look forward to continued engagement with the Administration and HHS on the Negotiation Program and on the important issue of lowering drug costs. Please contact Jennifer Reck, Director, NASHP Center on Drug Pricing, at jreck@nashp.org with any questions on these comments.

Respectfully submitted,

The National Academy for State Health Policy

April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Subject Line: Medicare Drug Price Negotiation Program
200 Independence Ave., SW
Washington, DC 20201

Submitted via email: IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Brooks-LaSure:

The National Association of Chain Drug Stores (NACDS) appreciates the opportunity to comment on CMS' Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026. On March 15, 2023, CMS issued a memorandum to provide initial guidance regarding the implementation of sections 11001 and 11002 of the Inflation Reduction Act (IRA), which establishes the Medicare Drug Price Negotiation Program ("Negotiation Program") to negotiate maximum fair prices (MFPs) for certain high expenditure, single source drugs and biologics for initial price applicability year of 2026.

NACDS represents traditional drug stores, supermarkets and mass merchants with pharmacies. Our chains operate nearly 40,000 pharmacies across the United States, and NACDS' chain member companies include regional chains, with a minimum of four stores, and national companies. They fill over 3 billion prescriptions yearly and help people use medicines correctly and safely, while offering innovative services that improve patient health and healthcare affordability.

I. Introduction

Under the initial guidance, CMS will select 10 negotiation-eligible Part D drugs for 2026 and publish a list of those drugs not later than September 1, 2023. The number of affected drugs will increase annually until reaching a total of 60 drugs for years 2029 and beyond. CMS intends to require that Primary Manufacturers, defined as the entity that holds the NDAs and BLAs of the selected drugs, provide two options to access to the MFP including ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP or issuing a retrospective reimbursement for the difference between the dispensing entity's acquisition cost and the MFP. As part of this obligation, the Primary Manufacturer

must ensure the MFP is made available to pharmacies for units of the selected drug for which there is a Secondary Manufacturer.

As CMS works to implement this Negotiation Program, CMS must utilize its full breadth of authority to ensure transparency, consistent oversight, and proper governance to protect all contracted entities in the MFP supply chain against unnecessary burdens, discriminatory practices, and arbitrary remuneration/fees (e.g., effective rates, transaction fees), particularly community pharmacies. To do this, CMS should use its authority to provide detailed guidance through program instruction.

CMS must not delegate authority to other stakeholders (e.g., manufacturers, pharmacy benefit managers) as this would be contrary to the intent of the IRA for CMS to negotiate lower prices with manufacturers and to provide patients with more affordable prescription drugs, and to do so without imposing burdens on other stakeholders in the prescription drug supply chain. To successfully achieve this, CMS must take the lead, be more prescriptive, and remove ambiguity about the operationalizing of this program and should continue to work with stakeholders after the April 14th deadline to resolve any outstanding issues in the supply chain. In other words, providing what is perceived to be free range to manufacturers would be contrary to the intent of the IRA.

Furthermore, the initial guidance has several gaps that need to be addressed that will require more than the allotted time to assess and resolve. As such, these comments represent our initial thoughts on CMS' initial guidance.

CMS also intends to require that a Primary Manufacturer ensure that pharmacies as well as intermediate entities, such as wholesalers, as applicable, are reimbursed timely for the full amount of the difference between their acquisition cost for the selected drug and the MFP within 14 days. **CMS is clear that manufacturers or their contracted entities shall not charge any transaction fee for this process.**

II. CMS Possesses the Authority to Collect MFPs Directly from Manufacturers

As mentioned above, in the initial guidance, CMS states its intention to require that Primary Manufacturers provide access to the MFP in one of two ways: (1) ensuring pharmacies can access the prescription drug at a price no greater than the MFP, or (2) providing retrospective payment for the difference between the pharmacy's acquisition cost and the MFP. CMS is proposing these two pathways because CMS is also proposing to define "providing access to the MFP," as required by section 1193(a)(1)(A), by ensuring that the amount paid by the pharmacy for the selected drug is no greater than the MFP.

NACDS respectfully requests that CMS reconsider these proposals and we offer workable alternatives that CMS should adopt. While NACDS recognizes that "ensuring that the amount paid by the pharmacy . . . is no greater than the MFP" could be achieved by options (1) or (2) above, these options would pose unnecessary burdens on the prescription drug supply chain, and most directly on pharmacies. We provide more detail about the unnecessary burdens in Section IV below.

Our recommendation is that CMS should collect directly from the Primary Manufacturer the difference between the MFP and the price CMS would pay but for the existence of the MFP (i.e., price without MFP or MFP rebate). This would be the simplest, cleanest, and most cost-effective mechanism for manufacturers to provide access to the MFP for the selected drug to pharmacies, mail-order facilities, and other dispensers with respect to MFP individuals who are dispensed the drugs, as it would impose the minimal possible burden on wholesalers, Part D plans, pharmacies and, most importantly, patients.

CMS clearly possesses the authority to require manufacturers to provide access to the MFP in this manner. On page 31 of the initial guidance, CMS states the following:

Under section 1860D-2(d)(1)(D) of the Act, as amended by section 11001(b) of the IRA, the negotiated prices used in payment by each Part D plan sponsor for each selected Part D drug must not exceed the applicable MFP plus any dispensing fees for such drug. In Part D, the negotiated price of a Part D drug is the basis for determining beneficiary cost-sharing and for benefits administration at the point of sale. Therefore, the requirement that the price used for beneficiary cost-sharing and benefits administration cannot exceed the MFP (plus dispensing fees) ensures that Part D MFP-eligible individuals will have access to the MFP at the point of sale. **Therefore, while section 1193(a)(1)(A) of the Act specifies that manufacturers must provide access to the MFP to MFP-eligible individuals, as a practical matter that will be accomplished by Part D plan sponsors without additional steps required of the manufacturer** (emphasis added).

Here, CMS recognizes that although the IRA requires manufacturers to provide access to the MFP to MFP-eligible individuals, the IRA does allow this to be accomplished by Part D plan sponsors without additional steps required of the manufacturer. Our proposed recommendation would follow a similar approach—manufacturers would provide access to the MFP to CMS, and then CMS would work with Part D plan sponsors not only without additional steps required by the manufacturer but also without additional steps required by other members of the supply chain and beneficiary care team.

III. Alternatively, CMS Should Bifurcate the Guidance so that Affected Industry Stakeholders may take the Time Necessary to Determine the Mechanics of how the MFP Should Flow to MFP-Eligible Individuals

NACDS respectfully requests that CMS consider providing stakeholders additional time to determine the best path forward with minimal pharmacy risk and burden (administrative and compliance) to implement the mechanics of the MFP. In the event that CMS chooses not to adopt our recommendation under Section II above, NACDS is requesting that the National Council for Prescription Drug Programs (NCPDP) convene a meeting of all relevant MFP implementation stakeholders to ensure all the stakeholders' concerns are addressed so that patients are not negatively impacted in 2026. NACDS appreciates CMS' willingness to continue working with stakeholders on MFP implementation after the April 14 comment

deadline, as CMS officials expressed on an April 5 pharmacy sector stakeholder call.

IV. NACDS' Third Alternative to Address Specific Concerns with the CMS Initial Guidance

Should CMS decide to reject both of NACDS' recommendations to either (1) collect MFPs directly from the Primary Manufacturer, or (2) bifurcate the initial guidance to give the industry time to determine the mechanics of the MFP flow to MFP-eligible individuals, then NACDS asks that CMS address our concerns by continuing to work with us to implement the recommendations and features below that will set the necessary guardrails to help ensure seamless experiences for beneficiaries at the point-of-sale and to help ensure their access to the pharmacy of their choice.

A. CMS Must Be Prescriptive in its Approach

CMS intends to require that the Primary Manufacturer ensure that pharmacies have access to the MFP. To implement this requirement, CMS proposes that a Primary Manufacturer would be required to submit its process for making the MFP available at least 30 days before the start of the price applicability year for the selected drug. CMS further intends to monitor compliance and audit, as needed, to ensure that the MFP is made available. NACDS finds CMS' proposals woefully inadequate and unworkable for pharmacies, for the numerous reasons detailed below.

1. For the Benefit of MFP-Eligible Individuals, CMS Must Establish Guidelines and Oversight

Under CMS' proposal, each manufacturer could impose its own process for making the MFP available to pharmacies. Pharmacies potentially would have to reconfigure their operations to accommodate multiple different processes from each manufacturer. Pharmacies do not have the resources and bandwidth to do this. Moreover, under CMS' proposal, pharmacies would have as few as 30 days to implement any necessary accommodations dictated by the manufacturers. Frankly, we are astounded that CMS believes that the nation's approximately 60,000 pharmacies, not to mention other dispensers, could accomplish these feats in as few as 30 days.

Rather than grant manufacturers *carte blanche* to design the MFP-availability processes using whatever discretion they desire, it is incumbent upon CMS to ensure a smooth, standardized, and seamless experience for MFP-eligible individuals by defining and establishing the MFP-availability process. Instead of delegating the responsibility of determining the MFP-availability process to each manufacturer, CMS itself should establish one process that all manufacturers must follow. CMS must impose manufacturer guardrails and retain oversight of the process to maintain the statute's intent and program integrity. Unless CMS determines specific roles and responsibilities that are standardized among and across manufacturers and throughout the pharmaceutical supply chain, including Part D plans and their associated PBMs, we cannot be certain that all pharmaceutical supply stakeholders would be able to comply to provide MFP-eligible individuals with timely access to the MFPs. The CMS-determined MFP process must provide specific guardrails to ensure consistent processes, payments, reporting, calculations,

protocols, timelines, and dispute resolution. Said another way, CMS should ensure accountability over the entity or entities that are responsible for ensuring that beneficiaries receive the MFP.

2. Pharmacy-Specific Concerns

To help ensure continued beneficiary access to the pharmacy of their choice, CMS needs to provide clarity on a number of matters that could affect pharmacy reimbursement so that pharmacies can remain confident in their ability to continue to serve Part D beneficiaries.

First, CMS must address the matter of acquisition cost versus reimbursement cost under the MFP model. CMS should clarify and establish guidelines on how pharmacies will receive transparent and reasonable reimbursement that includes a dispensing fee, as required under the IRA.

Second, CMS must clarify how the MFP mechanics and the prescription drug acquisition cost will be determined (e.g., WAC, NADAC) and fit into the MFP reimbursement structure for pharmacies. CMS should continue to work with stakeholders to ensure the intent of the IRA is accomplished and pharmacies are not forced to accept unreasonable and unfair reimbursements.

Third, CMS must establish protections to ensure that claims paid to pharmacies at the MFP are excluded from “effective rates” that Part D plans and PBMs impose on pharmacies. Of note, including the MFP claims in effective rate agreements would severely disadvantage pharmacies and lead to artificially low reimbursements by diluting pharmacies’ effective rates.

To help ensure continued beneficiary access to their preferred pharmacy, CMS must take steps that would minimize financial and operational burdens on all affected stakeholders, including pharmacies. Specifically, CMS:

- Must ensure pharmacies are not responsible for the compliance of other stakeholders in the process of providing the MFP to MFP-eligible individuals. In other words, CMS’ guardrails and oversight should allow pharmacies to be confident that beneficiaries’ coinsurance is accurately and properly calculated at the point-of-sale; and that pharmacies will be adequately and properly reimbursed pursuant to their Part D contracts.
- Must ensure that entities dispensing the MFP funds and involved in the MFP supply chain are held accountable and not imposing any direct or indirect fees or other remuneration demands or obligations on pharmacies. Of note, penalty guardrails may need to be considered to protect pharmacies from unsavory behavior in the prescription drug supply chain.
- Must ensure pharmacies can easily know and access MFP. All relevant information should be provided in a user-friendly manner that does not disrupt patient care.
- Must ensure there is a transparent and consistent appeals and dispute resolution processes for MFP if funds do not align with posted MFP calculations.

- Must ensure pharmacies are not pre-funding any of the MFP transactions under any circumstance. This responsibility should be delegated to those identified to effectuate the MFP.

3. NACDS Recommends a Retrospective Approach Instead of a Prospective Approach

As mentioned above, CMS' initial guidance proposes two mechanisms by which Primary Manufacturers would provide access to the MFP, (1) ensuring pharmacies can access the prescription drug at a price no greater than the MFP — a *prospective approach*; or (2) providing retrospective payment for the difference between the pharmacy's acquisition cost and the MFP — a *retrospective approach*.

CMS' proposed prospective approach would not be workable for NACDS member companies. When pharmacies purchase medications, they do not know which products ultimately will be dispensed to which patients. More specifically, when pharmacies purchase medications, they cannot predict which of those medications will be dispensed to MFP-eligible beneficiaries. Consequently, under CMS' proposed prospective approach, pharmacies would have to maintain separate inventories for MFP-eligible beneficiaries, either by maintaining a physical dedicated inventory or a virtual inventory for MFP-eligible beneficiaries. Either type of separate inventory would introduce undue burdens into pharmacy operations and financial positions. Moreover, this could lead to pharmacies' having to defend against potential claims of mismanagement and calls for greater oversight, as has been the experience with similar programs that utilize multiple pharmacy inventories. For these reasons, we urge CMS to reject a prospective approach.

Instead, NACDS recommends that CMS adopt a retrospective approach, as this type of approach would have fewer impacts on pharmacy operations and financials. Notably, a retrospective approach would maintain current pharmacy purchasing procedures. NACDS cautions, however, that a retrospective approach should not require pharmacies to fund the MFP upfront and then be reimbursed at a later date, and should not require pharmacies to have to pursue reimbursement from other stakeholders, whether it be from a manufacturer or another entity.

We propose a retrospective approach in which a refund is paid to the pharmacy upon claims submission so that the pharmacy is fully reimbursed at the point of sale through standard claims processes. We further propose that CMS establish an entity, similar to the TrOOP facilitator, which works with all relevant stakeholders to ensure that necessary processing and funding occur in real time following a pharmacy submitting a reimbursement claim. Such an entity could be referred to as an "MFP refund facilitator." This entity could track patients and eligibility, calculate pharmacy refunds, and do so in a timely manner so that pharmacies do not have to engage in "pay-and-chase" in order to be fully reimbursed. Moreover, manufacturers could pre-fund the "MFP refund facilitator," similar to how the TrOOP facilitator is presently pre-funded in the Coverage Gap Discount Program (CGDP). Finally, we would highlight for CMS that the CGDP has been a success largely because it is one standard process over which CMS has authority. We believe that CMS has the authority to establish an "MFP refund facilitator" or to expand the duties of an existing entity such as the TrOOP facilitator.

B. Additional Considerations

1. Reimbursement Timing

CMS' initial guidance indicates that pharmacies must be paid within 14 days. We appreciate CMS' addressing the need for a reasonable reimbursement timeframe upon which pharmacies may rely. However, in the initial guidance, CMS does not indicate when the 14-day clock would start. NACDS asks that CMS clarify that the 14-day clock would start when the pharmacy adjudicates the qualifying prescription drug claim to the Part D plan. This recommendation to begin at the point of adjudication is consistent with Part D prompt pay requirements and the language of the IRA that requires pharmacies to be reimbursed within a certain timeframe after the dispensing of a drug, which typically is contemporaneous with the adjudication of the drug claim.

2. 340B Program Concerns

In the initial guidance, CMS expresses a number of concerns about the operation of the MFP program with respect to the 340B Program, and most notably concerns about preventing duplicate discounts and procedures to determine which price is lower, the 340B Program price or the MFP.

As CMS works to issue final guidance, NACDS wishes to reiterate the comments we submitted to CMS on March 10, 2023, in response to CMS' "Initial Memorandum Implementation of Section 1860D-14B of the Social Security Act regarding Medicare Part D Drug Inflation Rebates paid by manufacturers," that CMS issued on February 9, 2023. Specifically, we urge CMS not to implicate pharmacies in the process of identifying and reconciling 340B claims for the manufacturer. Pharmacies should not be required to shoulder the responsibilities of manufacturers.

We wish to recommend, once again, that CMS establish a central clearinghouse to identify 340B transactions dispensed to Medicare Part D patients, similar to the model in Oregon. The 340B clearinghouse would function as a claims verifier by reviewing transactions to determine if the claim is subject to the 340B price. This is a role that 340B TPAs (third-party administrators) and split-billing vendors currently provide the market today. We believe the establishment of a 340B clearinghouse will be critical in the identification of 340B transactions. There is precedent for CMS using a clearinghouse in the Part D program, as CMS has contracted with a clearinghouse to serve as the TrOOP facilitation contractor since 2005. In fact, these functions could be accomplished by the MFP facilitator that we have recommended above.

Moreover, the 340B clearinghouse should be responsible for working with CMS and manufacturers to determine the lesser of the MFP or the 340B discount price for each MFP-eligible drug and provide the outcome of this analysis to all relevant entities, including manufacturers and pharmacies. CMS should provide oversight of the determination process and subsequent reconciliation and reporting processes so that there is assurance that 340B covered entities are providing the necessary data to CMS or the clearinghouse. This CMS oversight should also protect pharmacies from disruptive reimbursement

behaviors that could occur during the reconciliation of the MFP versus the 340B price. Please keep in mind the appropriate roles of the contract pharmacies and covered entities to ensure pharmacies are not inadvertently disadvantaged by the determination and reconciliation processes.

Finally, we note that the entity that operates the clearinghouse must be free from conflicts of interest. The contractor should have no incentive to minimize the use of 340B drugs for Part D beneficiaries and should be prohibited from using 340B claims information for purposes other than preventing duplicate discounts on Part D claims. In fact, the clearinghouse could be the same entity as our proposed MFP facilitator.

3. Data Sharing Requirements

As CMS considers our recommendations, we also ask that CMS be prescriptive and outline what specific data elements are needed for stakeholders to effectuate the MFP while being mindful of the administrative burden this could impose on pharmacies and others in the supply chain if new data elements are required.

Specifically, CMS should outline the minimum data requirements for the purpose of the MFP transaction and limit any attempt for plan sponsors, intermediaries, and other contracted entities in the MFP supply chain from broadening those data requirements and assessing fees to the pharmacy. Without the minimum standardized data requirements being set, entities at their discretion could request additional, unnecessary information from pharmacies for myriad reasons. This would likely impose unnecessary burdens on pharmacies and likely the entire supply chain. Additionally, data should be exclusive and confidential to the relevant entities for the purpose of the MFP transaction.

V. Conclusion

NACDS appreciates the opportunity to provide our perspectives and workable solutions to CMS' Negotiation Program beyond what is outlined in the initial guidance. Overall, the pharmacy community would like to see a path that involves the least disruptive option with minimal pharmacy risk and burden (administrative and compliance), and that incorporates the features outlined above to ensure patients maintain access to the lower MFP prices and the pharmacy of their choice. For questions or further discussion, please contact NACDS' Christie Boutte, Senior Vice President, Reimbursement, Innovation, and Advocacy, at CBoutte@NACDS.org or 703-837-4211.

Sincerely,

A handwritten signature in black ink, appearing to read "Steven C. Anderson". The signature is fluid and cursive, with a long horizontal stroke at the end.

Steven C. Anderson, FASAE, CAE, IOM
President and Chief Executive Officer
National Association of Chain Drug Stores

NCHR Public Comment – CMS Inflation Reduction Act

The National Center for Health Research (NCHR) appreciates the opportunity to submit public comments on the Centers for Medicare & Medicaid Services (CMS) Inflation Reduction Act (IRA) Initial Program Guidance. NCHR is a non-profit think tank that conducts, analyzes, and scrutinizes research on a range of health issues, with particular focus on which prevention strategies and treatments are most effective for which patients and consumers. We do not accept funding from companies that make products that are the subject of our work, so we have no conflicts of interest.

We greatly appreciate the efforts of CMS to fully implement the authorities provided by Congress in the Inflation Reduction Act (Pub. L. 117-169) to lower the costs of prescription drugs for beneficiaries through drug price negotiations. We have focused our comments below on key items within the initial program guidance including criteria to select drugs for negotiations, data reporting requirements for selected drug manufacturers, use of real-world evidence, and inclusion of research using surrogate endpoints to demonstrate effectiveness of alternative therapeutics and have highlighted specific considerations for CMS.

Use of Real-World Evidence

We agree with the inclusion of pharmaceutical alternative therapies to assist with establishing initial negotiated price. It is important to consider to what extent the selected drug and alternative therapies have been shown to be safe and effective among the Medicare population and to consider the quality of the data used to make the determinations. The guidance document states that CMS will review real-world evidence (RWE) in considering clinical benefit of a selected drug and evidence of therapeutic alternatives. RWE can be a valuable tool when used properly, however there are limitations that should be considered. The use of RWE requires access to unbiased data of a substantial number of patients that are demographically and medically similar to the U.S. Medicare population. Patient registries have been excellent sources of information in other countries, but there are numerous shortcomings for their use in the U.S. Registries have the potential to include a matched control group to evaluate a product's effectiveness and safety, but are unlikely to make such comparisons. Research has indicated that registries often miss confounding patient and medical center variables that were not evaluated but influenced outcomes.^[1] Further, access to information from registries is a major problem in the U.S., as most if not all registries are controlled by medical societies. These societies control the data collected as well as the data that they will make public to government agencies, or other researchers. Lastly, these registries typically include little, if any patient-reported outcomes, such as pain or quality of life, as well as lacking data on other adverse events which are needed to evaluate outcomes that truly matter to patients.

“Big Data” from billing records and electronic health records can also be used to determine very serious adverse events, but have several limitations.^{[2],[3]} It is not possible to determine if patients took medication as instructed or complied with instructions. Additionally, when patients report adverse effects, especially those that are subjective and relatively common, that

information is not always included in billing records or EHR, making it difficult to accurately evaluate the frequency of those events.

Use of Surrogate Endpoints

The document also states that CMS will consider “validated surrogate endpoints that predict a relevant health outcome” to determine the clinical benefit of the selected drug and therapeutic alternatives. There is not always agreement whether a surrogate endpoint is a consistently accurate predictor of clinical outcomes and CMS should take this into consideration when reviewing data based on surrogate endpoints, and rely on the preponderance of solid scientific evidence. Surrogate endpoints are used by manufacturers to obtain approval by the Food and Drug Administration (FDA). They are especially common for obtaining accelerated approval, almost always with the requirement that efficacy will be validated by confirmatory trials completed at a later date. For example, the drugs aducanumab and lecanumab were granted accelerated approval based on a reduction of amyloid plaque in the brain of patients with Alzheimer’s disease. However, numerous studies have suggested this endpoint does not reliably predict changes in cognition.^{[4],[5]} Additionally, confirmatory trials for drugs granted accelerated approval are often significantly delayed and fail to demonstrate meaningful, patient-centered outcomes, while the drug remains on the market.^{[6],[7]} We recommend CMS only use surrogate endpoint data to determine clinical benefit if there is data using patient-centered outcomes and very strong scientific evidence.

Drug Selection Criteria

We strongly agree with the process described in the guidance document detailing how eligible drugs will be determined. Specifically, we agree with the inclusion of any dose, delivery method, indication for different patient populations, or authorized generic drug as one single source drug. Manufacturers have often used changes in dosing, delivery method, or indication to extend the life of patents on a drug, often blocking access to lower cost generic competition for years. We also agree that CMS should select the drug exclusivity timeframe based on the initial indication of the product. This will help prevent manipulating the negotiation process through harmful practices of patent abuse in the future.

Data Reporting for Selection

We appreciate the extent to which CMS will consider different data items received by drug manufacturers to determine the maximum fair price (MFP). In addition to providing information publicly, it should be made clear how these various data items are being used to justify decision making. For example, how will data submitted by the manufacturer that shows they have yet to recoup the costs of Research and Development be used by CMS? The use of the data and information required to be reported by drug manufacturers must be clearly explained to the public to promote true transparency in the process.

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Chiquita Brooks-LaSure
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Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and
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Dear Ms. Brooks-LaSure and Dr. Seshamani,

Thank you for the opportunity to respond to your Solicitation of Comments for the March 15, 2023 initial guidance regarding the Medicare Drug Price Negotiation Program established under the Inflation Reduction Act (IRA).

By way of introduction, I am a senior fellow at the National Center for Public Policy Research, a nonprofit foundation dedicated to advancing free market solutions to public policy problems. I hope to provide insights that can help ensure the Negotiation Program's implementation does as little harm as possible to patients, providers, and researchers. To that end, I would like to raise several concerns about the guidance released last month.

First, the guidance imposes secrecy requirements that, at best, are at odds with good governance and, at worst, represent an unconstitutional infringement on free speech.

As you know, the [guidance dictates](#) that any information that CMS shares with a drug manufacturer during the negotiation process must remain confidential, and also that once a drug is no longer eligible for negotiations, the company must destroy all related documents -- including their own emails and other written communications -- within 30 days. CMS presumably proposed these requirements

to prevent manufacturers from communicating with each other, and the public, about the government's negotiating strategy and priorities. If the guidance is implemented, there'd be virtually no way for companies to document or publicize what they deem to be repeat abuses or flaws in the negotiation process.

Similarly, outside stakeholders -- especially patient groups and good governance watch dogs -- would have almost no insight into whether CMS is taking their viewpoints into account. The guidance would unreasonably restrict companies' First Amendment right to free speech, and would deprive the public at large of any real-time insight into the negotiation process, despite CMS's decisions having potentially life-or-death implications for millions of patients.

In fact, the lack of transparency -- coupled with the fact that the IRA prohibits judicial or administrative review of CMS's negotiating decisions -- is so egregious that it arguably deprives companies of due process.

It's very possible that decisions made under the Negotiation Program will force Medicare patients to stop taking medicines that are essential to maintaining their health in favor of far less effective alternatives. For this reason, I implore the agency to give patients and providers, in particular, a larger voice in how prices are determined.

The use of therapeutic reference pricing as the main basis for determining a drug's "maximum fair price" (MFP) is another cause for concern. To begin with, the guidance offers no clear criteria for judging what medicines count as "therapeutic alternatives." This makes it highly likely that the reference pricing process will ignore important clinical differences between a selected drug and what CMS deems a therapeutic alternative.

There's also nothing in the initial guidance to stop CMS from referencing a generic therapeutic alternative when setting the MFP for a brand-name drug, a comparison that will enable the agency to systematically undervalue state-of-the-art medicines.

Furthermore, according to the initial guidance, CMS "intends to consider the length of the available patents and exclusivities," when setting a medicine's price and that, in cases where a "selected drug has patents and exclusivities that will last for a number of years, CMS may consider adjusting the preliminary price downward."

One consequence of this policy is that it will discourage companies from doing additional research on medicines already approved by the FDA. Should a firm find a new application for an existing medicine -- and secure a new patent for that post-approval indication -- they could be vulnerable to more severe CMS price cuts

under the Negotiation Program. As a result, firms will have a significant disincentive to engage in such work.

This would have devastating consequences for innovation, as some of the most important and needed indications are often discovered after a drug has earned FDA approval. In the case of oncology drugs specifically, it's incredibly [common](#) for a medicine approved for one form of cancer to earn approval for treating another form of the disease. For these kinds of advances to occur, however, drug firms need to invest in expensive, time-consuming post-approval research. Under the current guidance, that research would dry up.

The IRA's Medicare Drug Price Negotiation Program has already introduced massive uncertainty into the drug development ecosystem. The initial guidance only adds to the uncertainty by establishing an unpredictable, non-transparent drug-pricing process in which patients, providers, and countless other stakeholders have almost no voice.

Thank you for the opportunity to share these concerns.

Sincerely,

Drew Johnson
Senior Fellow
National Center for Public Policy Research

Submitted electronically to IRAREbateandNegotiation@cms.hhs.gov

April 14, 2023

Meena Seshamani, M.D., Ph.D.
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Director of the Center for Medicare
Centers for Medicare & Medicaid Services
Department of Health and Human Services
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Re: Medicare Drug Price Negotiation Program Guidance

Deputy Administrator Seshamani,

The National Community Pharmacists Association (NCPA) appreciates the opportunity to provide feedback on CMS' *Medicare Drug Price Negotiation Program: [Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments.](#)*

NCPA represents America's community pharmacists, including 19,400 independent community pharmacies. Almost half of all community pharmacies provide long-term care services and play a critical role in ensuring patients have immediate access to medications in both community and long-term care (LTC) settings. Together, our members represent a \$78.5 billion healthcare marketplace, employ 240,000 individuals, and provide an expanding set of healthcare services to millions of patients every day. Our members are small business owners who are among America's most accessible healthcare providers.

NCPA supports the intention of the Inflation Reduction Act to lower patient's out-of-pocket costs. To further that end, NCPA supports having PBMs pass through rebates and discounts that they receive directly to patients, and has long supported state and federal legislation to require PBMs to implement a pass-through pricing model. Under the Medicare Drug Price Negotiation initial guidance, the basis for calculating patient cost sharing will be maximum fair price (MFP), not list price, which would be good for patients' out-of-pocket costs.

Community pharmacies are eager to serve an active role in implementing the Inflation Reduction Act. But for this initial guidance to work, and to preserve patient access to beneficiaries' pharmacy of choice to drugs under this guidance, pharmacies must be made whole to remain economically viable and maintain patient access to MFP drugs.

Independent pharmacies are integral to Part D plan network accessibility. The average independent pharmacy derives 36% of script volume from Part D, and LTC pharmacies derive 60 – 70% of script volume from Part D. Hundreds of pharmacies are closing each year, and the majority of these are independents, leading to pharmacy deserts. There are many causes for this, including vertical integration, PBMs steering to their affiliate pharmacies, below-cost reimbursement from PBMs, and restricted/preferred networks that block independent pharmacies.

At the same time, independent pharmacies are in pain and at an inflection point with increased stress from pharmacy DIR fees. Medicare Part D pharmacy DIR fees now account for approximately 5-6 percent of gross prescription revenue from *all* payers, representing the third highest expense after COGS (78%) and payroll (13.1%). According to MedPAC's March 2023 Report to Congress, pharmacy DIR fees were \$12.6 billion for 2021 (a \$3.1 billion (+33%) increase from \$9.5 billion in 2020).¹

Harmful DIR trends are only getting worse. For Medicare Part D CY24 contract offerings, our members are seeing approximate reimbursements at AWP-26% + \$0 dispensing fee (30ds) and AWP-31% + \$0 dispensing fee (90ds) for brands. These reimbursement rates represent pricing significantly below community pharmacies' cost to purchase brand drugs. Rates such as this coupled with year-over-year double-digit increases in DIR fees will make the first 3-6 months of 2024 unbearable for independent pharmacies, as they continue to pay DIR fees from CY23. Pharmacies will have to draw from more lines of credit/building reserves, and cash flow is a dire concern.

After reviewing the guidance, NCPA is unclear how pharmacies will ultimately be reimbursed for MFP-eligible drugs. For example, NCPA is unclear how pharmacies would be protected from losing money under the Medicare Drug Price Negotiation program. NCPA is concerned that pharmacies could experience negative cashflow when the actual acquisition cost of the medication to the pharmacy is more than reimbursement based on MFP. As MFP is the Part D negotiated price ceiling, the MFP could (and likely will) go lower at pharmacies' expense.

NCPA is concerned that this is essentially a pass-through model for pharmacy payment, without professional dispensing fee protections. We notice that pharmacies will be paid MFP plus "any" dispensing fee, making dispensing fees to pharmacies optional. It is crucial that CMS require dispensing fees that adequately cover the actual costs of dispensing the prescriptions. We believe that it is essential that pharmacy be engaged and compensated to cover costs of acquiring and dispensing drugs to make this program successful. Lastly, since there is no formal rulemaking, CMS will not conduct a small business impact analysis. How does CMS know the true impact of this guidance on small business community pharmacy?

¹ See [MedPAC March 2023 Report to the Congress: Medicare Payment Policy](#), page 399.

Below are our initial comments, subject to change as CMS develops its policy. When CMS has a more definitive policy on the Medicare Drug Price Negotiation program, the National Council for Prescription Drug Programs (NCPDP), could be a forum to discuss how NCPDP's standards can be used to effectuate these policies.

It will be important to identify new business processes that would be the most viable for the industry to operationalize to ensure that pharmacies have access to the MFP by 2026, and are made financially whole.

The Inflation Reduction Act created an exception to the non-interference in Part D clause in Section 1860D–11(i) of the Social Security Act (42 U.S.C. 1395w–111(i)), so that the Secretary of HHS “may not institute a price structure for the reimbursement of covered part D drugs, except as provided under part E of title XI” [the Medicare Drug Price Negotiation Program provisions].²

NCPA requests that CMS use this exception to establish a price structure for the Medicare Drug Price Negotiation Program, specifically a financially viable model of pharmacy reimbursement including but not limited to an MFP that accounts for margin on the ingredient cost of the drug, plus a required and economically viable professional dispensing fee, and to ensure that supply chain entities cannot impose terms on pharmacy including but not limited to pharmacy DIR fees on MFP drugs.

NCPA supports the following guiding principles to protect beneficiary access to independent pharmacy in the Medicare Drug Price Negotiation program:

- Pharmacy should not be responsible for the costs and related risks of operationalizing any MFP effectuation options
- Any entities responsible for payment effectuation should have a fiduciary responsibility to pharmacies
- CMS should consistently apply any MFP with CMS oversight, guardrails and governance
- All manufacturers must follow the same MFP structure of payment
- This guidance and its implementation should cause no disruption to pharmacy
- Plans, PBMs, manufacturers and wholesalers should not be able to disadvantage pharmacy
 - CMS should implement this guidance into seamless point of sale transactions
 - Pharmacies should not report acquisition cost nor reimbursement
 - Supply chain entities cannot impose additional MFP terms in pharmacy contracts
 - Plans/PBMs cannot steer or limit coverage of MFP drugs to affiliate pharmacies
 - Pharmacies should have reimbursement protections against egregious contracting practices such as BER (brand effective rate) clawbacks

² See Section 1198(b)(1)(C), at <https://www.congress.gov/117/plaws/publ169/PLAW-117publ169.pdf>, page 36.

- Pharmacies should not be loaning or floating money
- Pharmacy should not pay any fees to effectuate MFP
- Pharmacies should not be reporting using spreadsheets; any reporting should use NCPDP standards with automation in mind to maximize efficiencies
- Pharmacies should not fall victim to underwater payment on claims for MFP drugs/protections if MFP goes lower
- Pharmacies should be reimbursed commensurate professional dispensing fees
- Clear dispute resolution process for pharmacies regarding any grievances with supply chain entities
- Reimbursement for MFP drugs should not be subject to DIR fees/retrospective clawbacks

40.4 Providing Access to the MFP

According to the initial guidance, CMS intends to require that Primary Manufacturers provide access to the MFP in one of two ways: (1) ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP; or (2) providing retrospective reimbursement for the difference between the dispensing entity's acquisition cost and the MFP.

Feedback on option #1 (ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP)

NCPA has some reservations about this option, especially the likely need for pharmacies to have separate virtual inventory, like what exists under the 340B program. NCPA would appreciate CMS guidance on how it envisions the role of a virtual inventory as part of this option. NCPA is also aware that some partners in the supply chain would not favor option #1.

What our members do appreciate about this option is that it allows pharmacies to conserve cashflow and not be subjected to paying the wholesaler's regular price for the drug being dispensed for an MFP-eligible claim. Our members appreciate this option in that pharmacies would not be subject to loaning or floating money (i.e., through pharmacy paying a surplus payment that is later credited back to the pharmacy from the wholesaler, as highlighted in the Initial Guidance's "chargeback" example). Many of our members pay staff daily and weekly and have carrying costs. Furthermore, due to inflation and the time value of money, such chargebacks work against pharmacies.

If CMS moved forward with option #1, NCPA advises that CMS should ensure that plans pay a reasonable reimbursement rate that factors in the MFP, the actual costs of dispensing the drug, to avoid merely creating a product cost pass-through program that does not actually cover the pharmacy's operating costs. What is labeled a "dispensing fee" in the vast majority of Part D contracts is not adequate to cover the actual costs of dispensing a prescription. Claims paid under any option should be excluded from pharmacy direct and indirect remuneration (DIR) fees or retrospective clawbacks.

Concerns with option #2 (providing retrospective reimbursement for the difference between the dispensing entity's acquisition cost and the MFP)

NCPA has the following concerns with a wholesaler chargeback program to provide retrospective reimbursement.

Concerns with growing managerial control of pharmacy by wholesalers. With the implementation of DSCSA and controlled substance laws, among other factors, independent pharmacists are seeing wholesalers' managerial control of pharmacies grow. Furthermore, generic and brand compliance rates requiring a certain percentage of drugs be purchased from a given wholesaler make it so that pharmacies contract with wholesalers in a bundled, non-transparent fashion. If option #2 is done through a reconciliation process with the wholesalers, wholesalers will have even more managerial control over the revenue of pharmacies, and pharmacies would need to have added protections.

Concerns with wholesaler chargeback model. If CMS were to implement a wholesaler chargeback model, CMS should structure it so that pharmacy is assured it will be made financially whole. NCPA is concerned with the potential lack of transparency of a wholesaler chargeback model, with potential varying, convoluted, and non-transparent wholesaler fees, administrative costs, rebates and metrics. Furthermore, wholesalers are not HIPAA-covered entities and in the absence of a business associate agreement, do not have access to pharmacies' patient-specific claim-level transaction data. Entering into business associate agreements to disclose HIPAA protected health information is a risk as well as administrative burden for pharmacies, and they are justifiably wary of sharing claim data with wholesalers. Additionally, one pharmacy may have multiple wholesalers, which would greatly complicate the viability of a wholesaler chargeback model.

CMS provides the following example of how a chargeback would work:

For example, a pharmacy may purchase a medication for \$100 per bottle and the MFP as applied to this selected package is \$80. The Medicare beneficiary is enrolled in a Part D plan under which coverage of the selected drug is available, thus the beneficiary is an MFP-eligible individual. For this example, the plan has not negotiated a lower price for the medication. The pharmacy provides the negotiated price (i.e., MFP plus a dispensing fee) at the point of sale to the Medicare beneficiary. As a result of this transaction, the pharmacy is owed \$20 by the manufacturer. **The pharmacy would submit the information regarding the \$20 chargeback amount to its wholesaler and receive a credit from the wholesaler for that amount.** The wholesaler would be compensated by the manufacturer after billing the manufacturer for the chargeback amount. **[NCPA emphasis]**

Protections needed under wholesaler chargeback model. If CMS decides to go forward with such a model, NCPA strongly advocates for protections for pharmacy from wholesalers. NCPA would suggest the following:

- Wholesalers should bear the financial risk of creating, maintaining and operating any wholesaler clearinghouse and/or chargeback model;
- Pharmacies should be able to freely lodge complaints to CMS about wholesalers and others;
- Pharmacies should be paid with interest for the time between dispensing the MFP prescription and the time they are made whole, given the time value of money and inflation;
- CMS should integrate any chargebacks with the claims process, so as not to unduly burden pharmacies; and
- The chargeback should be automatically initiated following the pharmacy submission of a claim.
 - The pharmacy should not be burdened with initiating the chargeback process, as is given in CMS' example above (see bold text).
 - It is not feasible for pharmacies to evaluate RxBIN and RxPCN numbers to manage the process; pharmacies should not be expected to identify which BIN-PCN combinations tie to a Part D Plan and indicate in the claim they do or do not claim MFP reimbursement for the claim, as the list of combinations is large.³

In sum, NCPA does not support a wholesaler chargeback model to effectuate the MFP.

NCPA's Alternative Recommendations to Effectuate MFP

Proposal #1 - Central clearinghouse

The Medicare Drug Price Negotiation program could be processed by a central clearinghouse managed and governed by CMS, similar to Palmetto in the Medicare Part D coverage gap discount program. This would entail CMS providing PDE data to the facilitator, who then calculates the amount owed to the respective pharmacy, and then invoices the manufacturer, while pharmacies are paid at the same time the claim is adjudicated. The manufacturer could prefund payments for pharmacies. Pharmacy would be reimbursed based on the actual cost of dispensing the drug. This reimbursement would be based on publicly available benchmarks, where the clearinghouse would only need the NDC number, quantity dispensed, and claim identifier for each drug. No Protected Health Information under HIPAA, nor reimbursement fields, would be or need be shared. A fair and commensurate professional dispensing fee is needed, because Part D dispensing fees are oftentimes zero to pennies, offered in take it or leave it contract terms. Using a reference price established by the manufacturer such as WAC protects the confidential nature of an individual pharmacy's actual acquisition cost and is simpler to administer than trying to account for an individual pharmacy's prescription medication purchasing arrangements.

Such a clearinghouse should be a disinterested party, and should not be either a PBM or a wholesaler or related party. With a clearinghouse, a payment processor would be responsible for

³See <https://www.cms.gov/files/zip/binpcn2023.zip>.

processing and facilitating payment from the manufacturer to pharmacies. Payments should be transparent to the pharmacy and itemized at the claim-level on the 835 remittance advice. Pharmacies should not be charged any administrative or transaction fees.

Proposal #2 – Secondary claims adjudicator/MFP refund facilitator

The NCPDP Telecommunication standard is currently leveraged to offer an electronic voucher program for manufacturer copay discounts in the commercial plan marketplace. If pharmacies transmit a claim for a brand medication that is eligible for an electronic voucher, the switch knows it is a Medicare Part D claim (based on the Part D processor identification number (RxBIN) and Part D processor control number (RxPCN)), and the pharmacy receives a message that it is ineligible for an electronic voucher. The electronic voucher is currently unavailable in Medicare Part D.

The existing system could, through modified computer language and programming, similarly act to identify drugs in the Medicare Drug Price Negotiation program. A claims switch or processing facilitator could continue to reject Medicare Part D drugs, but not the drugs in the Medicare Drug Price Negotiation program. Claims could be adjudicated at point of sale, without needing full disclosure to PBMs and wholesalers.

A secondary claims adjudicator/MFP refund facilitator will not hurt cash flow for pharmacies. If set up correctly, no additional work is needed by the wholesalers, this process is very easy for pharmacies, and pharmacies are not required to submit additional data. However, this proposed electronic voucher program would need cooperation from the switch(s) and manufacturers.

Proposal #3 – CMS collects MFP directly from manufacturer

As an alternative option to the electronic voucher proposal above, CMS could collect directly from the Primary Manufacturer the difference between the MFP and the price CMS would pay but for the existence of the MFP (i.e., price without MFP or MFP rebate). This would be the simplest, cleanest, and most cost-effective mechanism for manufacturers to provide access to the MFP for the selected drug to pharmacies with respect to MFP individuals who are dispensed the drugs, as it would impose the minimal possible burden on wholesalers, Part D plans, pharmacies and, most importantly, patients. However, NCPA has concerns that pharmacy reimbursement would essentially be a product cost pass-through model in this proposal.

Proposal #4 – Separate NDC numbers

Manufacturers could create secondary NDCs for the drugs in the Medicare Drug Price Negotiation program, and make those NDCs available to wholesalers and system vendors at the MFP. Pre- and post- editing would catch them on matching, and using RxBIN and RxPCN numbers, these drugs could be paid on MFP plus a dispensing fee. We understand the concerns from manufacturers with setting up separate Medicare and non-Medicare NDCs, which is historically burdensome. We also understand the concerns manufacturers have with making this a prospective payment system that can result in misidentifying product resulting in mis-applied discounts.

NCPA Additional Comments, Concerns, and Recommendations

Pharmacy cannot be collateral damage to patients having access to MFP. NCPA has concerns about the economic viability of this guidance for pharmacies. Reimbursement for brand drugs is often solely based off AWP while purchasing of brand drugs is often based on the WAC published price. NCPA is concerned that pharmacy reimbursement for MFP eligible drugs may be inadequate for pharmacies, especially if there are not mandatory dispensing fees to factor in the actual cost of dispensing. Additionally, the MFP is the maximum negotiated price for these drugs in the Medicare Drug Price Negotiation Program, and CMS stated in the guidance that manufacturers can offer a price lower than the MFP for these drugs.

NCPA is concerned that the MFP is not financially sustainable for pharmacies. For example, NCPA does not see protections in this guidance preventing the PBM from reimbursing below MFP, nor preventing wholesalers from selling to pharmacy above MFP, nor preventing manufacturers for negotiating discounts off MFP which can lead to the MFP going lower than the negotiated price at the pharmacies' expense, all of which will affect pharmacy reimbursement and the ability of pharmacies to be made whole.

NCPA also has concerns that PBMs and commercial plans could adopt the MFP, which will be public, for those drugs, causing similar financial concerns for pharmacy stated above in non-Medicare Part D plans. Nevada has introduced [AB 250](#) which would broaden the applicability of MFP to apply to purchasers within the state, and similar states may follow.

Dispensing fees must be required and economically viable. **NCPA is concerned that under this guidance, pharmacies will not be compensated with a fair and commensurate professional dispensing fee.** According to CMS' Contract Year 2023 Policy and Technical Changes to the Medicare Advantage and Medicare Prescription Drug Benefit Programs final rule,⁴ effective January 1, 2024, the negotiated price includes any dispensing fees.⁵ CMS also stated in the initial guidance that "Under section 1860D-2(d)(1)(D) of the Act, as amended by section 11001(b) of the IRA, the negotiated prices used in payment by each Part D plan sponsor for each selected Part D drug must not exceed the applicable MFP plus any dispensing fees for such drug."

Dispensing fees may be included in current Part D contracts, but are not adequate to cover the cost of dispensing. Furthermore, Medicare Part D contracts are take-it-or-leave it to the

⁴ [2022-09375.pdf \(govinfo.gov\)](#), at 27899.

⁵ 423.100 Definitions. Negotiated price means the price for a covered Part D drug that— (1) The Part D sponsor (or other intermediary contracting organization) and the network dispensing pharmacy or other network dispensing provider have negotiated as the lowest possible reimbursement such network entity will receive, in total, for a particular drug; (2) Meets all of the following: (i) Includes all price concessions (as defined in this section) from network pharmacies or other network providers; (ii) Includes any dispensing fees; and (iii) Excludes additional contingent amounts, such as incentive fees, if these amounts increase prices; and (3) Is reduced by non-pharmacy price concessions and other direct or indirect remuneration that the Part D sponsor passes through to Part D enrollees at the point of sale.

pharmacy, leaving the pharmacy little choice but to accept unfair dispensing fees, however there may be opportunity for margin on the ingredient cost of the drug being dispensed to partially offset the virtually non-existent dispensing fees in Part D. However, not having a fair dispensing fee when there is no markup on the ingredient cost for MFP eligible drugs could result in pharmacies not stocking the drugs and therefore reducing access, as is the case with pharmacies reluctant to stock Paxlovid (pharmacies are not allowed to charge for the drug and thus rely solely on dispensing fees that more often than not do not cover the cost of dispensing the drug). Dispensing fees should be adequate as in fee-for-service Medicaid programs to cover the pharmacy's business operation costs, especially when dispensing MFP eligible drugs may lead to a complete pass-through reimbursement model for pharmacy on the ingredient cost portion of pharmacy reimbursement.

LTC pharmacy concerns. NCPA has additional concerns that LTC pharmacies will be disproportionately affected by this guidance, given LTC pharmacy's higher dispensing costs compared to the retail setting, based on following CMS' ten criteria for LTC pharmacy.

Acquisition cost. In its guidance, CMS states that it intends to require that Primary Manufacturers provide access to the MFP in one of two ways: (1) ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP; or (2) providing retrospective reimbursement for the difference between the dispensing entity's acquisition cost and the MFP.

NCPA opposes using pharmacy acquisition cost as proposed in the guidance. The acquisition cost proposal is a pass-through model which does not leave room to cover operating costs for the pharmacy, as pharmacies would be trued up to cost and most part D plans currently do not pay a dispensing fee, much less one based on the actual cost of dispensing the drug. Plus, pharmacy purchasing arrangements with their wholesaler vary. Trying to track down acquisition costs to the penny for nearly 20,000 independent pharmacies would be logistically difficult and burdensome. Using acquisition cost would cause disruption to the supply chain, and create misaligned incentives. For example, pharmacies disclosing acquisition costs would undermine contracting and could result in lower pharmacy reimbursement. Also, as discussed above, NCPA members are not supportive of a wholesaler chargeback model that would presumably be based on actual pharmacy acquisition cost. **Instead, we support CMS using a more widely reported reference price - WAC.**

Reasonable rate of reimbursement. In the Contract Year 2023 Policy and Technical Changes to the Medicare Advantage and Medicare Prescription Drug Benefit Programs final rule, CMS noted that many commenters requested that CMS establish safeguards to guarantee that pharmacies participating in Medicare Part D receive a "reasonable rate of reimbursement."⁶ CMS noted that these commenters urged the administration to ensure that the negotiated price at a minimum cover the pharmacy's costs of purchasing and dispensing covered items and providing covered services, and that some commenters requested that CMS establish a flat dispensing fee or an

⁶ See [2022-09375.pdf \(govinfo.gov\)](#) at 27845.

alternative such as pharmacy reimbursement based on a public drug pricing benchmark such as national average drug acquisition costs (NADAC) plus a fair dispensing fee in line with those in state Medicaid fee-for-service programs. In response, CMS stated that it would consider these suggestions for future rulemaking. **NCPA urges CMS to take this into consideration as the agency moves forward with implementation of the Medicare Drug Price Negotiation program.**

Reasonable and relevant terms and conditions. Furthermore, Part D plans are required to provide “reasonable and relevant terms and conditions of participation whereby any willing pharmacy may access the standard contract and participate as a network pharmacy.”⁷ **NCPA likewise urges CMS to take this into consideration as the agency moves forward with implementation of the Medicare Drug Price Negotiation program.**

Timely Reimbursement

NCPA appreciates CMS stating in the guidance that it intends to require that a Primary Manufacturer ensure that pharmacies and others are reimbursed timely for the full amount of the difference between their acquisition cost for the selected drug and the MFP within 14 days. **NCPA asks CMS clarification as to what the 14-day timeframe measures specifically. Does the 14-day clock start when the pharmacy adjudicates the qualifying prescription drug claim to the Part D plan?** This recommendation to begin at the point of adjudication is consistent with Part D prompt pay requirements and the language of the IRA that requires pharmacies to be reimbursed within a certain timeframe after the dispensing of a drug, which typically is contemporaneous with the adjudication of the drug claim.

Community pharmacies operate with very tight cashflows and cannot afford to float and loan money to supply chain entities. NCPA asks CMS to elaborate on the 14-day timeframe to ensure prompt payment to pharmacies, consistent with current Part D policy.

No Transaction Fee

CMS also states that manufacturers or their contracted entities shall not charge any transaction fee for this process, of which NCPA is appreciative. NCPA advises CMS to be wary of supply chain entities to circumvent the provision against transaction fees by charging “general claims processing” or “switch” fees. **NCPA advises that CMS elaborate on what constitutes a transaction fee for purposes of effectuating the MFP and have a clear mechanism for enforcement.**

40.4.1 Nonduplication with 340B Ceiling Price

NCPA believes it is imperative to avoid duplication of discounts between the 340B program and the Medicare Drug Price Negotiation program. Many of our members act as Contract Pharmacies for Covered Entities (CEs) but pharmacies are not the source of truth for determining the drug dispensed was eligible for 340B pricing. The way the 340B program is currently administered is too complicated to rely on an indicator for prescription claims and will result in inaccurate information. The current NCPDP Telecommunications Standard Version D.0 for pharmacy claims

⁷ [eCFR :: 42 CFR 423.505 -- Contract provisions.](#)

does not require a pharmacy to identify which prescription claims were dispensed using drugs purchased at a discount under the 340B program. Although the standard does include a field where a 340B indicator could be provided, it is optional for pharmacies to use, based on trading partner agreements. To proactively include a 340B identifier on a prescription claim, a pharmacy needs to know at the point of sale that the patient, their prescription and the parameters of their arrangement with the covered entity, qualify for the 340B program drug pricing. The indicator exists but there is a significant operational challenge to identifying when pharmacies should use it. Due to the multiple factors that go into determining that a drug dispensed is eligible for 340B pricing, it is not common for a pharmacy to know at the point of sale that a prescription could be dispensed with a 340B-priced drug.

CE Administrators are responsible for preventing our members from contributing to duplicate discounts. The CE should bear sole liability for any duplicate discounts, not the Contract Pharmacy. However, as NCPA has explained to CMS in past comments,⁸ there is significant administrative burden posed to pharmacies identifying 340B units both proactively and retroactively. **Instead, NCPA advises CMS either have a third-party administrator identify 340B units for CMS, or have manufacturers report aggregate, approximate 340B units to CMS.**

90.2 Monitoring of Access to the MFP

CMS states that it is the Primary Manufacturer's responsibility to ensure access to the MFP, and mentions that there are various methods by which pharmacies can determine whether they are accessing the MFP for a selected drug.

For example, the MFPs for selected drugs will be published by CMS, giving pharmacies an opportunity to know the MFP for each selected drug, as well as the explanation for each MFP. The MFPs for selected drugs for initial price applicability year 2026 must be published by September 1, 2024. In addition, CMS anticipates that pharmaceutical database companies will publish the MFPs such that they would become more readily accessible to pharmaceutical purchasers. CMS believes such transparency of the MFPs for selected drugs will help pharmacies to know the MFP for a selected drug and determine whether they are able to access the MFP. CMS is seeking comments on additional ways that CMS could help dispensing entities and MFP-eligible individuals know the MFP for a selected drug and determine whether they are able to access it.

First, if MFP is added to compendia drug files, the pharmacy dispensing system could also display the MFP. **Secondly, NCPA believes that wholesalers can put MFP information on their invoices and wholesaler catalogues.**

Chargebacks. CMS states that there is widespread use of chargeback payments and rebate mechanisms among the pharmaceutical stakeholders in the private sector, which allows for entities to receive rebates or discounts on their purchases after those purchases are made, based on the specific population to whom the drug or biological is dispensed. CMS also states that the

⁸ [comments-cms-part-d-inflation-rebatesL.pdf \(ncpa.org\)](https://www.ncpa.org/wp-content/uploads/2023/07/comments-cms-part-d-inflation-rebatesL.pdf)

private sector may make modifications to these existing mechanisms to effectuate access to the MFP. As referenced above, NCPA does not support a wholesaler chargeback model to effectuate the MFP. However, **in any chargeback structure of reimbursement, NCPA requests that credit memos must be available, and include claim reference identifiers to reconcile discounts. Remittance advices in the industry standard format (NCPDP standard 835) must be provided.**

Reporting issues. CMS stated that it intends to establish a process by which pharmacies would be able to report instances to CMS in which the MFP should have been made available to them but was not. CMS is seeking comment on how such a process would operate most effectively. **Under any wholesaler chargeback model, NCPA suggests that CMS communicate directly with wholesalers for this information, as most wholesalers have PSAOs, purchase drugs, and will control chargebacks in “option 2.” NCPA also requests that CMS provide guidance on what pharmacies should do if they believe that the chargebacks are inaccurate.**

NCPA also advises that CMS should provide guidance on a dispute/complaint process where pharmacies can initiate complaints for any model used to effectuate the MFP. CMS must have a streamlined, effective complaint process to ensure that disputes are resolved promptly to keep pharmacy’s solvent. No matter what model CMS decides to incorporate, chargeback or otherwise, pharmacies must have a way to report issues promptly and efficiently.

Conclusion

In summary, this initial guidance is being issued at a time when pharmacies are on the brink of closure. Medicare Part D plans and PBMs rarely pay dispensing fees, and Part D contracts are worsening. We have additional concerns that LTC pharmacies will be disproportionately affected by this guidance. NCPA is concerned that inadequate reimbursement could result in pharmacies not stocking drugs under the Medicare Drug Price Negotiation Program, which would reduce access.

NCPA thanks CMS for the opportunity to provide feedback, and we stand ready to work with CMS to offer possible solutions and ideas. Should you have any questions or concerns, please feel free to contact me at ronna.hauser@ncpa.org or (703) 838-2691, and my colleague Steve Postal, Director of Policy and Regulatory Affairs, at steve.postal@ncpa.org or (703) 600-1178.

Sincerely,



Ronna B. Hauser, PharmD
Senior Vice President, Policy & Pharmacy Affairs
National Community Pharmacists Association



April 14, 2023

Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Blvd
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments
Introduction

Dear Administrator Brooks-LaSure:

The National Health Council (NHC) thanks the Centers for Medicare & Medicaid Services (CMS) for the opportunity to comment on initial guidance for implementation of the Medicare Drug Price Negotiation Program for initial price applicability year (IPAY) 2026 as established by the Inflation Reduction Act (IRA).

Created by and for patient organizations over 100 years ago, the NHC brings diverse organizations together to forge consensus and drive patient-centered health policy. We promote increased access to affordable, high-value, equitable, and sustainable health care. Made up of more than 155 national health-related organizations and businesses, the NHC's core membership includes the nation's leading patient organizations. Other members include health-related associations and nonprofit organizations including the provider, research, and family caregiver communities; and businesses and organizations representing biopharmaceuticals, devices, diagnostics, generics, and payers.

As a patient advocacy organization whose mission is to promote increased patient access to affordable, high-value, sustainable, and equitable health care, we submit these comments regarding the impact of the negotiation program on patients. Our comments are informed by our concern for both patient access and affordability.

The NHC would first like to thank CMS for seeking feedback on the negotiation process guidance, a step that was not explicitly required in the IRA statute. While we would have preferred a more traditional Notice and Comment rulemaking opportunity that would ensure the Agency directly responds to stakeholder feedback, we welcome this opportunity to express our reactions to CMS' thinking on the negotiation program. As overarching priorities, the NHC urges CMS to craft the negotiation process to assure:

- Patient organizations have ample opportunity and ability to provide feedback on the negotiation process;

- CMS communicates how external data was factored into decisions, including methodology used;
- Patients have greater access and affordability of needed medicines; and
- Appropriate guardrails and ongoing oversight processes are established to study the impact of the negotiation program to protect patients and inform refinement of the program.

§10: External Data Submission Timing

The NHC understands the tight timeline for the drug selection and price negotiation processes. However, for patients to fully realize benefits of the negotiation program and to limit unintended consequences, CMS must provide ample time for patients to share data and experiences pertaining to selected drugs. The NHC is concerned that 30 days to submit data after CMS releases the list of drugs to be negotiated is insufficient time for organizations, who do not have research and/or data analysis departments and staff to collect information, to submit data that is most beneficial to CMS. We ask CMS to take the burden of data collection and submission into account as it evaluates the proposed timeframe for data submissions.

The NHC believes that CMS should extend the timeframe for stakeholders to submit requested data. At a minimum, the NHC requests that information can still be submitted throughout the negotiation process and could inform “second/final offer” decisions. CMS must consider the patient voice and perspective as vital to the negotiation process.

§50.2 and §60.3.3: Patient Engagement and Utilizing Patient Experience Data

The NHC has long championed the incorporation of patient perspectives in medical product research, development, and coverage. Patient engagement is an important step to better understand the burden of their condition, desired treatment outcomes, and views on benefits and risks. Driven by the work of the Food and Drug Administration on patient-focused drug development (PFDD), many companies in the biopharmaceutical community have devoted significant resources to better understand patient populations and are working to bring to market products that best suit their needs. While patients will benefit from lower-priced medicines, it is important for CMS to consider the positive impact it can have on PFDD if companies are rewarded for demonstrating that their products represent therapeutic advancements over other products and meet unmet needs identified as the most important to patients.

In addition to our earlier expressed concern about the short timeframe for data submissions, we ask CMS to provide more clarity on how the agency intends to leverage negotiation data elements outlined in §50.2 to ensure that the agency is evaluating these elements with the patients' experiences, preferred outcomes, and needs in mind. For instance, we ask CMS to transparently outline a consistent methodology for how data related to therapeutic alternatives will result in changes to an initial or final offer. As part of this methodology, we ask that CMS ensure data explicitly related to patient value is prioritized. We also ask CMS to emphasize patient experience and value in the evaluation of data.

We applaud CMS's reference to patient experience in its discussion of the clinical benefits of selected drugs and their therapeutic alternatives in § 60.3.3. Defining patient experience in this context and appropriately translating it to a drug's MFP is incredibly important. The NHC urges CMS to consider the following six domains of patient centered engagement and methodological practices as included in the NHC [*Rubric to Capture the Patient Voice: A Guide to Incorporating the Patient Voice into the Health Ecosystem*](#). The rubric was designed through a multi-stakeholder process to elevate meaningful patient engagement and ensure patient voice inclusion is seen in studies and that engagement includes:

- Patient Partnership;
- Transparency;
- Representativeness;
- Diversity;
- Outcomes Patients Care About;
- Patient-Centered Data Sources and Methods; and
- Timeliness.

Additionally, the NHC urges CMS to prioritize patient experience and patient experience data among the many factors the Agency identifies in the guidance as sources that will inform an initial/final offer. Specifically, CMS should ensure that among the data sets that inform any initial or final offer, patient experience data should have an outsized impact. CMS should also articulate how patient experience data influenced initial and final offers.

The NHC appreciates that CMS will consider evidence about alternative treatments to the selected drug, specifically on the categories included in the statute and identified in the guidance, including whether it is a therapeutic advance, FDA approval, effects on specific populations, and addressing unmet needs.

While we understand CMS must adhere to the requirements of the statute, we feel the approach taken in this guidance may represent a very narrow interpretation and could be defined in a way that takes a more holistic view to determine patients' views on the value of drugs compared to their alternatives. CMS is required to consider evidence about therapeutic alternatives to the selected drug, as available. This includes whether it represents a therapeutic advance; prescribing information; comparative effectiveness, including effects on specific populations; and whether it addresses an unmet need. We encourage CMS to consider what evidence may be needed for each identified category and support the broadest scope of evidence that may be considered. For example, when considering whether a product represents a therapeutic advance, it is important to consider whether the advance is based on outcomes important to patients, including non-clinical outcomes such as productivity or independence. The patient community is well suited to collect and provide this type of information, though a more thorough approach to patient engagement, as explained below, will help CMS better understand a range of elements important to patients to help direct patient organizations toward data that will best suit CMS' needs.

Need for Broader, Consistent Patient Engagement

In addition to the opportunity to submit data, the NHC urges CMS to develop further initiatives to solicit feedback from the patient community. These processes could be comparable to the FDA's work in PFDD.¹

CMS should develop a patient engagement infrastructure that creates an ongoing dialogue about IRA implementation and systemic issues with those most affected by them. This can include:

- Creating a patient ombudsman charged with oversight of implementation;
- Convening public roundtables of disease or treatment-specific experts from the patient and disability communities for each drug selected for MFP negotiation; and
- An Administrator-level Patient Advisory Committee to provide overall feedback on this program and other work of the Agency.

This infrastructure could help patients and caregivers provide input to CMS about domains that will inform negotiations such as:

- The impact of the condition on patients and their family caregivers, and how it affects their daily activities, physical functions, and quality of life – overall and across key domains: social, physical, emotional, and functional;
- Outcomes that are most important to the patient, both clinical and non-clinical (e.g., goals, daily activities, symptom reduction, or a standard of quality of life);
- Patients' preferences for treatment delivery methods and views on beneficial and negative aspects of treatment effects; and
- Experience on treatment(s) including symptoms and side effects and how the treatment impacts their daily activities, physical functions, and quality of life.

Throughout this process, CMS should be sure to solicit input from diverse communities in order to gain information about the differences among subpopulations and their needs, outcomes, and preferences.

NHC Resources

In addition to the Rubric mentioned above, the NHC has several tools that can help identify and infuse the patient experience into the value discussion. These include the [Patient Experience Mapping Toolbox](#), which was developed to help researchers capture patient experience data more holistically and in a standardized manner across chronic diseases. The Toolbox includes project planning and data collection tools.² We have also created a Blueprint for the development of [Patient-Centered Core Impact Sets \(PC-CIS\)](#), which address

¹ "Externally-Led Patient-Focused Drug Development Meetings." U.S. Food and Drug Administration, FDA, 29 July 2022, <https://www.fda.gov/industry/prescription-drug-user-fee-amendments/externally-led-patient-focused-drugdevelopment-meeting>

² All patient-facing tools in the Toolbox were reviewed externally by health literacy experts and refined through patient interviews. To encourage uptake, the Toolbox is made available free for public use.

inconsistencies between what is important to patients and the information that is typically collected in research and care. A PC-CIS is a standardized, patient-derived, and patient-prioritized list of the most important impacts - both clinical and non-clinical - a disease and/or its treatments have on a patient's health and daily life, and that of their family and caregivers.

§50.2 and §60.3.3: Utilization of Quality-Adjusted Life-Years (QALYs) in the Negotiation Process

The NHC greatly appreciates CMS stating that it will not use metrics such as QALYs. Any evidence that values extending the life of some individuals less than extending the life of other individuals based on disability status, age, or other special populations (e.g., children or those of marginalized status, including the patient community of color) is completely inappropriate. All patients deserve to be treated equally, and thus we laud CMS' adherence to the statute and decision to separate out and exclude QALY metrics from data that otherwise factor in QALYs. However, we are concerned that CMS may not effectively eliminate QALYs from analysis by utilizing studies that use QALY-related data from secondary sources, or that CMS may over-exclude analyses that are otherwise helpful in establishing the value of a drug. Therefore, the NHC requests that CMS offer more clarity into exactly how it will exclude QALY-based metrics from analysis of certain evidence in value-based decisions. The NHC also requests that CMS highlight when and how the agency removed QALY-based metrics from consideration in MFP justification documentation.

While it is clear both in the statute and this guidance that QALYs will not be used as a base for evaluations, CMS requests input on what other measures might be appropriate or inappropriate. While the NHC does not have positions on other specific measures, we do think that it is important that CMS not rely on a single metric and look at a wide variety of sources to take a holistic approach to this data. One potential approach to aggregate the different dimensions of value is multi-criteria decision analysis. As discussed in the NHC's 2020 white paper on the topic,³ patient value is multi-faceted, and any attempts to distill important dimensions of patient value and benefit into a single number is fraught. We recommend the negotiation process leverage metrics that are driven by patient experience data and patient input and are patient-centered.

§60: Input Process for Future Program Guidance

The NHC appreciates the opportunity to comment on initial program guidance for IPAY 2026 and seeks clarification on processes for seeking feedback moving forward. The NHC requests insight on what opportunities CMS plans to put forward for stakeholders to provide formal input into adjusting future program guidance and whether there will be a comment opportunity to inform negotiation for IPAY 2027 and beyond. The NHC believes that CMS may need to reevaluate methodology for various pieces of the negotiation process, including aggregating drugs to determine MFP. The negotiation program is a new policy that is being implemented in a non-traditional manner. As such, the NHC believes CMS should be nimble and responsive to

³ <https://nationalhealthcouncil.org/additional-resources/patient-centered-multi-criteria-decision-analysis/>

feedback from stakeholders and the policy is implemented in future years. To do so, CMS should establish a meaningful process for 1) patients and other stakeholder to provide consistent feedback on the experience of IPAY2026 and 2) CMS to evaluate policy decisions made for the initial year of negotiation and incorporate necessary changes quickly for future years.

§ 60.6.1 Explanation for the MFP

The explanation for the MFP will be a critical tool in the continuous improvement of the negotiation program, as well as a tool the patient advocacy community will use to learn and improve our ability to participate in the process. We urge CMS to assure that these explanations are clear, accessible, and transparently available. We also ask that they include critical information about what data was used to develop the MFP and how specifically it was used. We are especially interested in information about how patient experience data was incorporated and weighed against other factors. Including this information in the explanation will help patient advocates develop the most useful data for future negotiations.

We also note that CMS' March 1, 2025 deadline for publishing explanations of 2026 MFPs coincides with deadlines for stakeholders to submit information on selected drugs for IPAY 2027, which will make it difficult for stakeholders to glean insight from the explanations to refine and improve their data. We urge CMS to reevaluate the timeline for releasing the explanation to encourage improved stakeholder submissions.

§110: Requirements for Coverage

While the patient community is incredibly supportive of the Part D redesign and out-of-pocket cap, we understand plans will face higher liability moving forward. These shifting incentives, combined with potentially changed market dynamics created by the negotiation process, make it more important than ever that CMS ensure access to medicines and create guardrails such as limiting burdensome barriers such as prior authorization and step therapy. While some utilization management protocols may be grounded in sound clinical decision making, such as prior authorization to limit drug-to-drug interactions or to prevent overprescribing of potentially addictive medication, the development of such protocols is typically done without much or any patient input, and the rationale for such decisions is not typically made public. By defining coverage requirements more explicitly, CMS reduces the risk of plans denying coverage for products vital to a patient's comprehensive care plan. If a plan is receiving a lower price based on a maximum *fair* price, the benefit should be fully conveyed to beneficiaries through *fair* access. Conversely, it is crucial CMS continuously work to ensure access and remove barriers to both negotiated and non-negotiated drugs that providers and patients agree are necessary and appropriate.

Moving forward, the NHC believes that it will be important for CMS to clearly outline a definition of coverage requirements, either in this guidance and/or in any upcoming Part D regulations and payment rules. Appropriate guardrails should be established to assure that patients are, at the very least, no worse off in terms of access than they previously were.

Overarching Comment: Oversight and Continuous Improvement

Given the significant impact this new program and other changes such as the redesign of the Part D program will have on the drug delivery system, CMS must have proper systems in place to monitor impacts to ensure implementation of the IRA achieves our shared goal of increasing access and affordability for patients. At a minimum, CMS should monitor whether people see the savings they are expecting, whether future plan designs inappropriately restrict access to either negotiated or non-negotiated drugs, including through increased utilization management, and the creation of other barriers to access. And while this guidance only applies to Part D drugs, one additional consideration for the Part B program will be monitoring prescribing behaviors to ensure there are not incentives for providers to prescribe non-negotiated products. Furthermore, CMS should monitor the impact of drug selection criteria to ensure it is not creating disincentives to conduct follow-on research on additional indications or new formulations that can demonstrate additional benefit such as greater adherence or reduced side effects.

CMS has made it clear that this guidance is only for the first year of negotiation, and there likely will be the need for adjustment as the mechanisms are put in place. We recommend CMS undertake a formal process for seeking input from patients on the impacts of IRA implementation soon after full implementation and regularly after that. This will help identify areas of concern such as those listed above and identify any needed adjustment.

Additional Comments on Drug Selection

Although we are aware that you are issuing Section 30 on drug selection as final, we have a few comments we hope CMS will consider as you implement the drug selection process for negotiation.


For example, we are concerned about the effects that aggregation of drugs with the same active moiety or active ingredient in the selection process could have on subsequent research. We want to make sure that manufacturers aren't discouraged from developing new indications and forms of administration that may improve patient adherence and/or outcomes. Without appropriate guardrails, CMS' broad definition of drugs eligible for negotiation may discourage these types of improvements. While manufacturers would ideally bring products to market with as many indications as possible, one potential consequence could be a significant delay in initial market entry and access. The NHC is aligned with CMS' desire to eliminate potential gaming of extending patent life or time before negotiation. However, we fear this may be an overly broad approach that does not consider the patient perspective on whether new formulations or forms of administration improve patient care and believe there are better approaches to address this issue. If CMS is unable to reconsider this approach, we request that you undertake future notice and comment processes with adequate time for stakeholders to consider the impact of selection criteria as the negotiation process is implemented.

Conclusion

The NHC strongly upholds that decisions on value should be driven by the patient perspective. The best results occur when patient organizations can engage and when patients are not limited by policies that restrict access to products that best meet their individual needs. The NHC urges CMS to carefully consider these comments for this and future guidance and allow for patient voices to be heard and emphasized throughout the negotiation process.

The NHC thanks CMS for the opportunity to provide input on this important issue. Please do not hesitate to contact Eric Gascho, Senior Vice President of Policy and Government Affairs, if you or your staff would like to discuss these comments in greater detail. He is reachable via e-mail at egascho@nhcouncil.org.

Sincerely,

A handwritten signature in black ink that reads "Randall L. Rutta". The signature is written in a cursive, flowing style.

Randall L. Rutta
Chief Executive Officer



April 10, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attn: PO Box 8016

Re: Medicare Drug Price Negotiation Program Guidance

Submitted via email: IRAREbateandNegotiation@cms.hhs.gov

Dear Administrator Seshamani:

The National Hispanic Council on Aging (NHCOA) urges you to reconsider your released implementation guidance for the Drug Price Negotiation Program within the Inflation Reduction Act (IRA). This program adversely impacts medical innovation and access to critical medicines relied upon by countless seniors under Medicare Part D. Minority communities, including Hispanic seniors, would unduly suffer as a result of fewer medical breakthroughs. The IRA's price-setting program works against the scientific community's charge in bringing about new medicines that help underserved communities overcome barriers to higher-quality healthcare. As an organization dedicated to the well-being of older Hispanic Americans, our concerns with CMS' implementation of the IRA are numerous.

For one, the guidance fails to take into account the health equity learnings in recent years. As we emerged from the COVID-19 pandemic, the unique health challenges faced by minority communities were made evident to many. In 2022, NHCOA conducted a poll of Black and Hispanic voters in which we found that half of voters of color experience barriers to care when it comes to our healthcare.¹ Price setting provisions in the IRA would drastically disincentivize innovations in medicines, which can be helpful in overcoming barriers to care for certain conditions. Our country must work hard to ensure that minority communities, including Hispanic seniors, are able to better access the medicines they need. This guidance does not provide details on how it would remove barriers to care.

In addition, the language surrounding Medicare Part D, in particular, would greatly harm Hispanic seniors enrolled in the program. By artificially mandating drugs to be sold at a certain price, the ability of manufacturers to produce at levels to meet critical demands would be significantly strained. With fewer incentives to invest in innovation, research and development efforts would be

¹ National Hispanic Council on Aging & National Minority Quality Forum (2022). Results for 2022 Poll Among National Voters. <https://nhcoa.org/wp-content/uploads/2022/05/NHCOA-and-NMQF-Polling-Memo-2.pdf>



reined in, and Medicare beneficiaries would ultimately have fewer treatment and therapy options available to them.

This disruption of Medicare Part D, as outlined, demonstrates a failure to recognize the true ways we can address the challenges older Hispanics face when it comes to healthcare. Our government ought to ensure that drug middlemen pass discounts and rebates to patients, that copay accumulators are eliminated, and that PBM price hiking practices are thwarted. If we are serious about helping seniors afford their treatments, implementing these meaningful solutions would be prioritized.

Once again, we urge you to reconsider the elements of this guidance and take into consideration the potential consequences it will have on communities of color, especially seniors. We urge you to work closely with stakeholder and patient groups to find ways to truly explore solutions to address the barriers to care in the healthcare system, particularly those of communities of color and older adults.

Sincerely,

Dr. Yanira Cruz
President and CEO
The National Hispanic Council on Aging



The Nation's Advocacy Voice for In-Office
Infusion

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www.infusioncenter.org ▪ info@infusioncenter.org

April 13, 2023

RE: Medicare Drug Price Negotiation Program Guidance

Submitted via IRAREbateandNegotiation@cms.hhs.gov

The National Infusion Center Association (NICA) is a nonprofit organization formed to support non-hospital, community-based infusion centers caring for patients in need of provider-administered medications. To improve access to medical benefit drugs that treat complex, rare, and chronic diseases, we work to ensure that patients can access these drugs in safe, more efficient, and cost-effective alternatives to hospital care settings. NICA supports policies that improve drug affordability for beneficiaries, increase price transparency, reduce disparities in quality of care and safety across care settings, and enable care delivery in the highest-quality, lowest-cost setting.

Thank you for the opportunity to comment on the March 15, 2023 Memorandum entitled "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments."

As we expressed to the Congress throughout the legislative process leading to enactment of *Build Back Better*, we are concerned that, if the Medicare Drug Price Negotiation Program is administered on a prospective basis for Part B drugs, providers will be left underwater for medications subject to the new maximum fair price (MFP) mechanism. While the legislation attempted to ensure that purchasing providers can access the MFP, there is no guarantee of that in the complex world of pharmaceutical middlemen, nor is there any way to ensure that providers who cannot access the MFP are made financially whole. In light of these concerns, we urge CMS to implement the MFP mechanism in a retrospective manner, by which the drug company would reimburse Medicare for the amount by which its average sales price (or other metric as specified by the legislation) exceeds the MFP.

Office-based and ambulatory infusion centers play a key role as the most efficient setting for drug administration, compared to hospital outpatient departments and, in many cases, even compared to the home. Recently, the Employee Benefit Research Institute (EBRI) quantified the cost differences in healthcare services by site of treatment, including for the delivery of specialty medications. The EBRI report found that, "[I]f site-of-treatment price differentials for specialty medications were eliminated,



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employers and workers would save as much as 36 percent, depending on the medication.”¹ Reducing our nation's in-office drug administration capacity would be a counterproductive step if the goal is to reduce drug spending while still ensuring that patients can access complex drug administration in high-quality, low-cost settings. We are concerned that leaving providers underwater for MFP medications would cause such a reduction in capacity. A loss or consolidation of community-based infusion access points would have the effect of driving patients into the hospital for infusion, which is by far the most expensive setting: for some of the medications studied by EBRI, the hospital outpatient department charges were *more than double* those of office-based administration. This has an impact on our overall drug spending, but it also impacts patients, whose cost-sharing reflects these differentials.

That is why we urge CMS to administer the MFPs via a retrospective rebating process, which would avoid inadvertent disruptions to the office-based delivery channel by leaving providers out of the mechanism entirely. That would meet the twofold goal of delivering deep savings for Medicare, while protecting patient access to provider-administered medications.

Thank you for your consideration. If there is any additional information I can provide, please do not hesitate to contact me.

Sincerely,

A handwritten signature in black ink that reads 'Brian Nyquist'. The signature is fluid and cursive, with the first name 'Brian' and last name 'Nyquist' clearly legible.

Brian Nyquist, MPH
President and Chief Executive Officer
National Infusion Center Association

¹ EBRI Issue Brief No. 525: “[Location, Location, Location: Cost Differences in Health Care Services by Site of Treatment — A Closer Look at Lab, Imaging, and Specialty Medications](#)” by Paul Fronstin, Ph.D., Employee Benefit Research Institute, and M. Christopher Roebuck, Ph.D., RxEconomics, LLC (Feb. 18, 2021).



April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
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Attn: PO Box 8016

Re: "Medicare Drug Price Negotiation Program Guidance."

Submitted via email: IRAREbateandNegotiation@cms.hhs.gov

Dear Administrator Seshamani:

The National Minority Quality Forum (NMQF) welcomes this opportunity to share perspectives and comments for improving the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026.

NMQF is a research and educational organization dedicated to reducing patient risk by assuring optimal care for all. We are a not-for-profit, nonpartisan organization that integrates data and expertise in support of initiatives to eliminate health disparities. NMQF's vision is an American health services research, delivery, and financing system whose operating principle is to reduce patient risk for amenable morbidity and mortality while improving quality of life.

We come to these comments with the historic knowledge that the voices of concern from the Health Equity Movement about design failures in major Medicare initiatives have largely been ignored. As a result, structural flaws have translated into increased risk for poor health outcomes for millions of minorities and persistent inequities in the program are common. There is an extensive body of peer-reviewed literature that documents these disparities in nearly all phases of the program. By way of an example, attached is an annotated bibliography with over 10,000 references to racial and ethnic disparities in the Medicare program dating back to the 1970s.

Against this backdrop, we are encouraged by President Biden's January 20, 2021 "Executive Order on Advancing Racial Equity and Support for Underserved Communities Through the Federal Government," and February 16, 2023 "Executive Order on Further Advancing Racial Equity and Support for Underserved Communities Through The Federal Government" which state,

April 14, 2023

“Our Nation deserves an ambitious whole-of-government equity agenda that matches the scale of the opportunities and challenges that we face...It is therefore the policy of my Administration that the Federal Government should pursue a comprehensive approach to advancing equity for all, including people of color and others who have been historically underserved, marginalized, and adversely affected by persistent poverty and inequality. Affirmatively advancing equity, civil rights, racial justice, and equal opportunity is the responsibility of the whole of our government. Because advancing equity requires a systematic approach to embedding fairness in decision-making processes, executive departments, and agencies (agencies) must recognize and work to redress inequities in their policies and programs that serve as barriers to equal opportunity.”

This comprehensive approach must mean an enduring collaboration between the Center for Medicare and Medicaid Services (CMS) and all the communities that it serves. The Biden administration’s commitment to equity has given us great hope.

The Inflation Reduction Act (IRA) of 2022 is bringing sweeping changes to Medicare including the new Medicare Drug Price Negotiation Program¹. The IRA offers an opportunity to advance equity in the Medicare program. We support, for example, the IRA provisions that could benefit patients, including a \$2,000 cap on out-of-pocket-expenses, the expansion in eligibility of the Part D low-income drug subsidy, and the elimination of enrollee cost-sharing for vaccines. Yet, there is still more that can be done to address inequities in Medicare.

In this comment letter, we want to not only remind CMS administrators that historic inequities exist in the program that were not resolved by prior administrations and that their work should be guided by the President’s executive order. What gives us pause is that the released guidance offers little insight as to whether equity will be addressed in the implementation, and how success in that regard will be measured. Certainly, the significant changes contemplated by the drug negotiation provisions offer an opportunity to address longstanding disparities in Medicare.

NMQF respectfully requests that CMS align its implementation plans with the President’s executive orders. CMS has an opportunity to improve equity in Medicare, and if done, it should release to the public documentation that celebrates this historic change. CMS in its planning and implementation should ensure that it is not elevating risks of poor outcomes for minorities as demonstrated in decades of evidence. Most importantly, beneficiary risk mitigation must be the prime directive. By this commitment to equity, CMS can move us toward cementing an end to disparities in healthcare by providing better care for all Americans.

We hope that this comment letter invites a shared dialogue on how we can better examine and

¹ Centers for Medicare & Medicaid Services. “Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments” March 15, 2023

Letter to Administrator Seshamani

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April 14, 2023

address disparities in the program. We offer here to be a resource to help ensure that Inflation Reduction Act implementation does not expand the peer-reviewed literature on inequities in Medicare.

Sincerely,

Gary A. Puckrein, PhD

President and Chief Executive Officer

The National Minority Quality Forum



April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Meena Seshamani, M.D., Ph.D.
Deputy Administrator and Director of the Center
for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Dear Administrator Brooks-LaSure and Dr. Seshamani,

On behalf of the more than 25 million Americans living with one or more of the over 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) thanks the Centers for Medicare and Medicaid Services (CMS) for their extensive engagement with the rare disease community around implementation of the Inflation Reduction Act (IRA). NORD appreciates this opportunity to provide comments on the draft guidance 'Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191- 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments,' hereafter referred to as the "Negotiation Program" guidance.

NORD is a unique federation of non-profits and health organizations dedicated to improving the health and well-being of people living with rare diseases. NORD was founded 40 years ago, after the passage of the Orphan Drug Act (ODA), to formalize the coalition of patient advocacy groups that were instrumental in passing that landmark law. Our mission has always been and continues to be to improve the health and well-being of people with rare diseases by driving advances in care, research, and policy.

NORD appreciates CMS' willingness in the Negotiation Program guidance (Section 30.1.1) to consider additional actions to "best support orphan drug development" and is pleased to submit these comments to help CMS make good on its commitment to the rare disease community. These comments are intended to supplement and expand on the April 14th comment letter submitted by NORD and 100 other patient advocacy organizations that support rare disease patients (available in the appendix).

For many Americans living with a rare disease, out of pocket prescription drug costs create significant financial barriers and hinder patient access to needed therapies. Key provisions in the IRA, including the \$2,000 annual and amortized monthly caps on out-of-pocket costs for Medicare Part D beneficiaries, as well as expanded eligibility for financial assistance for low-income beneficiaries, ensure that more rare disease patients on Medicare will be able to afford the life-altering therapies they need. Robust patient education, particularly about the opt-in requirement to the smoothing mechanism, will be critical to ensuring patients have access to and benefit from these provisions of the IRA. While outside the scope of this guidance, NORD would welcome the opportunity to partner with CMS to help educate the rare disease community as IRA-authorized benefits become available to Medicare beneficiaries at the appropriate time.

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As implemented under the draft guidance, however, the Negotiation Program may adversely impact rare disease drug development. Before the Orphan Drug Act was enacted in 1983, fewer than 40 Food and Drug Administration (FDA) approved therapies were available to treat rare diseases.¹ Thanks to the ODA, rare disease therapies now consistently account for more than half of FDA approvals for new molecular entities.² Still, more than 90% of the more than 7,000 known rare diseases do not have an FDA approved treatment, making continued investment in rare disease research and innovation critical to the rare disease community.³ The section 1192(e)(3) exclusion for orphan drugs approved to treat a single rare disease could help sustain this innovation, as will the broader exclusion for “low spend” drugs with less than \$200 million in annual Medicare spending. However, the small patient populations and medical complexity associated with rare diseases create unique challenges to drug development. These small population sizes and complex, heterogenous disease manifestations also result in a more limited availability of data on issues such as clinical benefit and therapeutic alternatives, making it more difficult to determine a fair negotiated price for drugs that treat rare diseases compared to other therapies. Therefore, NORD appreciates the opportunity to highlight additional ways that CMS, consistent with the statute, can further support rare disease drug development in implementing the Negotiation Program.

Successful Negotiation Program implementation hinges on a careful balance between greater affordability and maintaining appropriate incentives for continued rare disease drug development. NORD urges CMS to address four areas of concern in future guidance:

1. Actively engage patients and create opportunities to provide meaningful data and insights;
2. Ensure rare disease patients have access to the negotiated therapies;
3. Further clarify the scope and timing of the orphan drug exclusion; and
4. Begin tracking the impact of the IRA on innovation and patient outcomes now.

Specifically, CMS should take the following steps to support rare disease patients and families:

1. Expand and strengthen data collection and engagement opportunities to ensure patients can meaningfully contribute their unique insights on the negotiated drug and its alternatives.

NORD commends CMS’ efforts to consider data on clinical benefit, therapeutic alternatives, and unmet medical need in the negotiation process and to incorporate relevant patient and provider perspectives. NORD thanks CMS for recognizing, in section 60 of the draft guidance, the unique and nuanced value orphan drugs can bring to specific subsets of the patient population, including those with few or no therapeutic alternatives. The agency’s stated objective to assess value in an indication-specific manner, including some off-label uses, is critical for CMS to fully understand and account for the complex treatment trade-offs and unmet needs that exist within the rare disease patient community.

Moreover, we are encouraged that the draft guidance explicitly recognizes the value of patient experience data, including its nuances, in section 60.3.3, and that not all patients are necessarily sharing the same

¹ Orphan Drugs In The United States: An Examination of Patents and Orphan Drug Exclusivity (2021): available at https://rarediseases.org/wp-content/uploads/2022/10/NORD-Avalere-Report-2021_FNL-1.pdf; accessed 4/2023

² New Drugs at FDA: CDER’s New Molecular Entities and New Therapeutic Biological Products; available at: <https://www.fda.gov/drugs/development-approval-process-drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products>; accessed 4/2023

³ Larkindale J, Betourne A, Borens A, Boulanger V, Theurer Crider V, Gavin P, Burton J, Liwski R, Romero K, Walls R, Barrett JS. Innovations in Therapy Development for Rare Diseases Through the Rare Disease Cures Accelerator-Data and Analytics Platform. *Ther Innov Regul Sci*. 2022 Sep;56(5):768-776. doi: 10.1007/s43441-022-00408-x.

views and experiences. For instance, the science of patient engagement has long recognized that patient experience data may reflect differences depending on disease progression or a patient's cultural, geographic, and socio-economic background. While we are grateful CMS recognizes the value of patient experience data, we strongly encourage CMS to expand the opportunities and strengthen the processes for providing such input to the agency as part of the negotiation process.

NORD is concerned that CMS' proposed approach would make it essentially impossible for patients and providers to submit meaningful data. CMS plans to largely rely on voluntary, public data submissions, on very short timelines, without meaningful data standardization, using complicated forms written at too-advanced reading levels and through hard-to-navigate processes that are neither intuitive nor patient-friendly. Patients will either not become aware of data collection efforts in time, or struggle to navigate the complex submission process. In addition, the required attestations are worded in a way that will likely discourage many patients from submitting data. To the extent patients will feel compelled to submit data containing Personal Identifiable Information (PII) and Personal Health Information (PHI), the data collection also raises privacy concerns.

Moreover, NORD foresees challenges in aggregating and analyzing individual patient and provider experience data submitted through this process. The data will be collected without a sampling frame and likely not representative while the collection method essentially makes it impossible to determine or account for such inherent biases in the data. In addition, the lack of standardized questions and scientific rigor will likely render this data largely anecdotal. This would contrast sharply with appropriate qualitative and/or quantitative research methodologies that would collect information in a scientifically rigorous and reproducible manner. A good example of such rigorous approaches is data collected through the FDA's patient-focused drug development (PFDD) meetings or patient surveys. Specifically, FDA's "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input" guidance⁴ provides detailed and tangible advice on operationalizing and standardizing data collection and data management in ways that are feasible for the rare disease patient community.

CMS will have to refine its proposed approach to incorporate meaningful external data sources. CMS plans to supplement the aforementioned data submitted by the public with relevant published data retrievable through literature searches. Unfortunately, for many rare diseases, data relevant to determine a negotiated drug's clinical benefit, therapeutic alternatives, or unmet medical need does not currently exist in peer-reviewed journals or consensus treatment guidelines. Additionally, the lack of disease-specific International Classification of Disease (ICD-10) codes for most rare diseases makes Real-World Data (RWD) sources such as Electronic Health Records (EHRs) or medical claims data largely infeasible for many rare diseases. This is a recognized challenge within rare diseases.

FDA's Voice of the Patient (VOIP) reports are designed to address this data scarcity and are critical to patient-focused drug development by assembling meaningful information on how patients evaluate therapeutic alternatives or characterize the unmet need and clinical benefit of alternatives. However, these data are not indexed in a way that would clearly find them in a traditional literature search. CMS should consider all relevant data collected as part of the FDA approval process in the negotiation process. Moreover, patient and provider engagement will be critical to ensure CMS is aware of and able to leverage all other available and relevant data sources regardless of how they are indexed.

⁴ FDA GFI: Patient-Focused Drug Development: Collecting Comprehensive and Representative Input; available at <https://www.fda.gov/media/139088/download>; accessed 4/2023

CMS will consequently have to collect data on treatment alternatives, clinical benefits, and unmet medical need for rare diseases *de novo*, including from patients, caregivers, and providers. Patients and caregivers have key insights on issues such as determining the value of a therapy and how it compares to potential alternate treatment options. Rare disease patients are often uniquely positioned to share the challenges associated with unmet medical needs - when there are no or very few options available to treat their condition - and the benefits to themselves, their families, and the community from a safe and effective therapy. Patient experience data will be particularly important given CMS' desire to evaluate drug prices on an indication-specific level including certain off-label uses, which are common in the rare disease space albeit notoriously hard to study.⁵ Because published data to assess these specific uses remain scarce, patients and providers are often the best experts from which to elicit such information related to rare disease treatments.

For the reasons outlined above, NORD urges CMS to:

a. Simplify and streamline the data submission process for patients, caregivers, and providers to eliminate barriers to their providing the requested information. This should include pre-testing the forms, attestations, and instructions with representatives of the relevant community to ensure they are clearly understood and easy to navigate, including by individuals with visual and other impairments. Because this data submission is voluntary and not subject to the 30-day statutory data submission timeline for mandatory manufacturer-provided data, CMS should work with the patient community to establish feasible timelines that will be workable for the community. FDA listening sessions, PFDD meetings, and other FDA-led initiatives routinely collect meaningful patient experience data in ways that works for rare disease patients and families and can serve as another valuable guide and resource for CMS, including all applicable attestations and data protections.

b. Clarify what information the agency is seeking from patients to allow data standardization and aggregation. The short time for submitting data makes it imperative to provide detailed instructions as early as possible, before the negotiation period begins, to facilitate and streamline the collection and submission of meaningful data. Clarifying the key data elements ahead of time will also empower patient advocacy groups and other important stakeholders to proactively collect and collate relevant information in a way that is scientifically rigorous and representative of the relevant patient community.

c. Organize CMS-led patient listening sessions specific to selected drugs to collect representative data within the different drug indications to inform CMS' initial offer for a negotiated drug. In planning for these sessions, CMS should use FDA patient listening sessions as a roadmap and work closely with the various impacted patient communities to develop a representative and meaningful data collection effort. For instance, while we appreciate why CMS intends to only focus on pharmaceutical alternatives and to primarily consider alternatives in the same drug class, we recognize non-pharmaceutical options such as surgery are often the only viable alternative for our patient populations and that therapeutic alternatives in other drug classes and with other mechanisms of actions may in fact be the most appropriate alternatives for some of our patients. Engaging the patient community in planning the listening sessions will help ensure that these alternatives are appropriately considered. Close collaboration with FDA will enable CMS to benefit from FDA's relevant best practices and extensive experience.

⁵ Fung A, Yue X, Wigle PR, Guo JJ. Off-label medication use in rare pediatric diseases in the United States. *Intractable Rare Dis Res.* 2021 Nov;10(4):238-245. doi: 10.5582/irdr.2021.01104. PMID: 34877235; PMCID: PMC8630459.

d. Include consistent and granular summaries of the data and assumptions on which each negotiation was based, including patient experience data. We urge CMS to report a detailed and standardized summary of the data relied upon in the negotiation process including the therapeutic alternatives, clinical benefit, off-label use, and unmet need for each indication and the data sources relied upon. CMS should further break out the use of patient experience data and patient-reported outcomes; list data identified by CMS through literature searches and guideline review; and identify primary data, such as claims, electronic health record (EHR), or other real-world-evidence, generated and collated by CMS. This level of transparency will be important to create consistency and trust in the negotiation process. Clearly breaking out the use of different data sources will also motivate the creation of valuable data sources including patient experience data for future negotiation years. In fact, much of the data for rare diseases collected through this process will be unique and have value beyond this specific negotiation process.

2. Give negotiated drugs a preferred place on the formulary and minimize utilization burdens to ensure patients have ready access to the negotiated drugs.

NORD supports section 1860D-4(b)(3)(I) of the Social Security Act which will require Medicare Part D negotiated drugs to be included on Part D plan formularies. However, we encourage CMS to take additional steps to ensure rare disease patients benefit from reduced out-of-pocket expenses associated with better formulary tier placement and to better assure their timely access to negotiated drugs through reduced utilization management processes.

Often, rare disease drugs are placed on the non-preferred or specialty tiers of Medicare Part D plan formularies, resulting in significant out-of-pocket costs and access delays. For instance, a study published in the *American Journal of Managed Care* (AJMC) in 2020 found “on average, 85% of orphan drugs on a [Medicare Part D] formulary were placed on its highest cost-sharing tier.”⁶ Similarly, a KFF analysis of 2023 Medicare Part D plans found that in 12 of the 16 the national prescription drug plans, coinsurance amounts for non-preferred drugs range from 40% to 50%, showing similar trends as in previous plan years.⁷ Moreover, 44% of these plans’ enrollees will face coinsurance ranging from 15% to 25% for preferred brands⁸, meaning less predictable and often higher out of pocket costs for patients compared to flat copays. KFF also found that the median coinsurance for drugs on the specialty tier was 25%.⁹

Another common source of treatment delays or denials for rare disease patients is related to prior authorization and step therapy. NORD believes health care providers, in partnership with their patients, are best positioned to choose the right therapy to treat the often-complex health care challenges faced by those with a rare disease. Yet, a 2020 study found that a staggering 76% of orphan drugs on Medicare Part D formularies were subject to prior authorization.¹⁰ Similarly, a 2021 study¹¹ found that nearly 40

⁶ Yehia, F., Segal, J.B. Predictors of Orphan Drug Coverage Restrictions in Medicare Part D. 2020 Sep; AJMC 26(09); accessible at <https://www.ajmc.com/view/predictors-of-orphan-drug-coverage-restrictions-in-medicare-part-d>

⁷ Kaiser Family Foundation (KFF): Medicare Part D: A First Look at Medicare Drug Plans in 2023; available at: <https://www.kff.org/medicare/issue-brief/medicare-part-d-a-first-look-at-medicare-drug-plans-in-2023/>; accessed 4/2023

⁸ Kaiser Family Foundation (KFF): Medicare Part D: A First Look at Medicare Drug Plans in 2023; available at: <https://www.kff.org/medicare/issue-brief/medicare-part-d-a-first-look-at-medicare-drug-plans-in-2023/>; accessed 4/2023

⁹ Ibid.

¹⁰ Yehia, F., Segal, J.B. Predictors of Orphan Drug Coverage Restrictions in Medicare Part D. 2020 Sep; AJMC 26(09); accessible at <https://www.ajmc.com/view/predictors-of-orphan-drug-coverage-restrictions-in-medicare-part-d>

¹¹ Lenahan, K.L., Nichols, D.E., Gertler, R.M., Chambers, J.D.: Variations in Use and Content of Prescription Drug Step Therapy Protocols, Within and Across health Plans. 2021, Nov; Health Affairs 40(11); <https://doi.org/10.1377/hlthaff.2021.00822>; available at <https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2021.00822>

percent of the specialty drugs offered within the 17 largest commercial health plans included step therapy in the drug coverage plan. Additionally, 55.6 percent of the step therapy protocols were found to be more stringent than clinical guidelines,¹² delaying timely patient access to appropriate care.¹³

From CMS' perspective, negotiated drugs will have been appropriately valued and therefore, we encourage CMS to:

a. Require that a negotiated drug be placed on a higher formulary tier to improve patient access through further reduced patient out-of-pocket costs. While the \$2,000 annual out-of-pocket cap and the smoothing mechanism to spread a patient's out-of-pocket costs out over the plan year will be tremendously helpful to Medicare patients living with a rare disease, coinsurance makes it more difficult for patients to predict their out-of-pocket expenditures. Requiring a negotiated drug's placement on formulary tiers that typically have copays instead of coinsurance can assist patients with both planning for prescription drug expenses and their ability to pay for their medications at the time they need them.

b. Significantly reduce or eliminate step therapy and prior authorization barriers in Medicare Part B and Medicare Part D for negotiated drugs. To further ensure timely access to these drugs, NORD urges CMS to include utilization management protections for negotiated drugs that have been determined by CMS to be appropriately priced. In the 2024 Medicare Advantage and Part D Final Rule (CMS-4201-F) released on April 5, 2023, and effective for the CY 2024 plan year, CMS will require "an approval granted through prior authorization processes must be valid for as long as medically necessary to avoid disruptions in care in accordance with applicable coverage criteria, the patient's medical history, and the treating provider's recommendation, and that plans provide a minimum 90-day transition period when an enrollee who is currently undergoing an active course of treatment switches to a new MA plan."¹⁴ NORD encourages the adoption of these or similar requirements for negotiated drugs offered on traditional Medicare Part D plan formularies as well.

3. Ensure CMS' interpretation of the orphan drug exclusion protects vital incentives for rare disease drug development

While the IRA includes a limited exclusion for orphan drugs that only treat one rare disease from drug price negotiation, NORD is greatly concerned with the potential impact of CMS' proposed interpretation of the exclusion on future innovation in rare disease drug development. Today, about 60 percent of all orphan drugs have a single FDA-approved indication, whereas only about 20 percent are FDA-approved for both orphan and non-orphan indications.¹⁵ Among the drugs that only have orphan indications, fewer than a quarter have more than one FDA-approved indication and fewer than 10 percent have three or more approved indications.¹⁶ Similarly, among the drugs that have both orphan and non-orphan indications, less than 20 percent have 3 or more orphan indications. This indicates that to date, relatively few orphan drugs have been successfully developed for more than one disease.

¹² Ibid.

¹³ Ibid.

¹⁴ Centers for Medicare & Medicaid Services (CMS); RIN 0938-AU96 Medicare Program; Contract Year 2024 Policy and Technical Changes to the Medicare Advantage Program, Medicare Prescription Drug Benefit Program, Medicare Cost Plan Program, and Programs of All-Inclusive Care for the Elderly; available at <https://public-inspection.federalregister.gov/2023-07115.pdf>; accessed 4/2023

¹⁵ IQVIA: Orphan Drugs in the United States. 2020; Dec; available at: <https://rarediseases.org/wp-content/uploads/2022/10/orphan-drugs-in-the-united-states-NRD-2020.pdf>; accessed 4/2023

¹⁶ Ibid.

Still, developing already-approved therapies to treat additional rare diseases is a critical strategy to address the rare disease community's significant unmet need because these drugs have already proven to be safe for humans. In fact, according to a recent analysis, over 3,000 unique drugs have been FDA-designated as rare disease drugs and studied, with about a quarter of these drugs being designated for more than one rare disease.¹⁷ Serial innovation and the investigation and development of multiple rare disease indications of use is an increasingly important dimension of orphan drug development, making the preservation of incentives to further develop drugs to treat additional orphan diseases after they have entered the market particularly important.

NORD also recognizes that relatively few orphan-only drugs will meet the annual revenue threshold of \$200,000,000 in combined expenditures under Medicare Parts B and D to make a drug negotiation-eligible. However, due to the complexity and long timeline from initial drug discovery and early research and development to FDA approval, drug sponsors are making decisions today that will impact their investments and drug development pipeline for decades to come. Remaining uncertainty about if, when, and how rare disease drugs will become negotiation eligible creates real business risks that work as strong disincentives to develop drugs for the limited populations impacted by rare diseases. Therefore, as part of the negotiation process, NORD urges CMS to make clear that research and development efforts in support of innovative therapies that help address unmet needs will be treated favorably in the price negotiation process.

We thank CMS for clarifying in the draft guidance that an orphan drug with multiple FDA-approved indications within the scope of an orphan drug designation for one rare disease (i.e., multiple indications tied to one orphan designation as shown in **Example 1**) remains excluded from negotiation. As a result, drug sponsors will consequently not be discouraged or penalized for further developing a rare disease drug for new sub-populations, such as children, or specific disease subtypes.

Example 1 - Orphan drug with one designation & multiple associated approved indications; CMS already clarified this is excluded from negotiation; this example was selected to be illustrative while reflecting common trends in orphan drug approvals.

Drug 1 (one designation, multiple FDA-approved indications)			
Designations		FDA Approved Indications	
Disease	Year	Year	Population
Rare Disease A	2014	2015	12 years and older
		2016	6 years and older
		1018	2 years and older
		2022	1 year and older

However, NORD is gravely concerned that CMS' interpretation of the orphan drug exclusion might contravene the intent of the ODA by discouraging drug sponsors from developing their drug for additional rare diseases. Specifically, CMS' interpretation of the IRA makes drugs eligible for negotiation as soon as they have been designated under section 526 of the Federal Food, Drug, and Cosmetic Act

¹⁷ Miller, KL, Kraft, S, Ipe, A, and Fermaglich, L. Drugs and biologics receiving FDA orphan drug designation: an analysis of the most frequently designated products and their repositioning strategies. Expert Opin Orphan Drugs. 2022 Mar 1;9(11-12):265-272. doi: 10.1080/21678707.2021.2047021.

(FFD&C) for more than one orphan disease – even if the drug is not actually FDA approved (or indicated) to treat more than one of the designated orphan diseases. For instance, consider **Example 2** and the many other rare disease drugs with similar regulatory history; although this drug has been designated for five different rare diseases, it is only FDA approved to treat a single orphan disease.

Example 2: Orphan drug with multiple designations and one FDA-approved indication; CMS should clarify that that this drug will be excluded from negotiation because while it has five designations, it only has one approved indication.

Drug 2 (multiple designations, one FDA-approved indication)

Disease	Designation Year	FDA Approval Year
Rare Disease B	2007	2017
Rare Disease C	2009	-
Rare Disease D	2016	-
Rare Disease E	2018	-
Rare Disease F	2019	-

Designating an orphan drug under section 526 of the FFD&C Act is done early in the drug development process and much earlier than submission of a New Drug Application (NDA) or Biological License Application (BLA). Orphan drug designation is critical to access to ODA incentives such as funding and tax credits for clinical research to help de-risk this phase of drug development. However, an orphan drug designation does not allow the company to market the drug; it is only the first in many steps towards approval and marketing. In fact, FDA’s Orphan Drug Designations and Approvals database currently contains 6,445 orphan drug designations (including withdrawn designations) compared to only 1130 approved orphan indications, demonstrating that a vast majority of orphan drug designations do not result in any FDA-approved indications – and therefore are largely irrelevant to the pricing considerations central to the Negotiation Program.¹⁸

NORD understands that the language of section 1192(e)(3), due to the manner in which it was drafted, is ambiguous and therefore open to CMS interpretation. CMS states that to qualify for the orphan drug exclusion, “the drug or biological drug must (1) be designated as a drug for only one rare disease or condition under section 526 of the FFD&C Act and (2) be approved by the FDA for only one or more indications within such designated rare disease or condition.”¹⁹ This two-prong test, embodying two separate and distinct criteria, is a possible interpretation of the statute. But under the canons of legislative drafting, if the congressional authors had intended the two clauses to be read *independently*, the proper legislative drafting would have structured the two clauses separately and in sequence. Instead, Congress did not separate the clauses, intending them to be read *together*: that a drug designated for a given “rare disease or condition” has “only [one] approved indication” or multiple “approved... indications” *within the scope of that designation*. CMS substantiates this plain meaning²⁰ of the provision in accepting that

¹⁸ US FDA Orphan Drug Designations and Approvals database; available at <https://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm>; accessed 4/2023

¹⁹ Meena Seshamani, Memorandum to Interested Parties: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments, March 15, 2023, at 10-11.

²⁰ E.g., *Sebelius v. Cloer*, 569 U.S. ___, No. 12-236, slip op. (May 20, 2013).

an orphan drug with **multiple** (“one or more”) FDA-approved indications qualifies for the exclusion provided all such approved indications are within the scope of a **single** (“only one”) **designation**.

A two-prong test also does not best reflect and advance the purposes and function of the Negotiation Program. The cardinal rule of statutory construction is that the whole statute should be drawn upon as necessary, with its various parts being interpreted within their broader statutory context in a manner that furthers statutory purposes.²¹ The proper interpretation of the orphan drug exclusion “in a manner consistent with [the] legislative purposes”²² of the Negotiation Program preserves an intentionally narrow class of qualifying orphan drugs determined upon the basis of a drug’s FDA **approval history** – not on orphan drug designations which have no bearing on, or applicability to, prescription drug marketing or pricing.

In considering the regulatory history for the drug shown in **Example 3**, the approval for Disease H in 2014 should trigger the drug becoming negotiation eligible (assuming it meets the other statutory requirements outlined in the IRA), rather than the Designation for Diseases H or I in 2010, thus preserving vital rare disease research and development incentives. One of the critical “additional actions” that CMS can take to support rare disease research and development would be to revise its guidance to reflect a sound statutory interpretation more fully in line with congressional intent to make an orphan drug negotiation eligible once it has been approved (or indicated) to treat a second disease.

Example 3: Orphan drug with multiple designations and multiple FDA-approved indications; CMS should clarify that an orphan drug with multiple designations and approved indications becomes negotiation eligible when the drug is approved for the second disease (in this example 2014) – NOT upon second designation in 2010.

Drug 3 (multiple designations & multiple FDA-approved indications)

Disease	Designation Year	FDA Approval Year
Rare Disease G	2008	2011
Rare Disease H	2010	2014
Rare Disease I	2010	-
Rare Disease J	2013	-

NORD is also concerned about the potential chilling effect residual uncertainty about CMS’s implementation of the orphan drug exclusion will have on rare disease drug development. CMS remains silent as to when orphan drugs that receive FDA approval for a second disease and therefore lose eligibility for the orphan drug exclusion would become negotiation eligible. Qualifying single-source drugs must have been approved at least 7 years and qualifying single-source biologics must have been licensed at least 11 years to qualify, but CMS has not yet clarified if the 7 or 11 years will be counted beginning on the date of the FDA approval for the second disease that made the drug negotiation eligible or based on the first orphan drug approval. CMS should clarify that obtaining additional designations for a small molecule or biologic will not make a drug negotiation eligible until the drug has been approved by

²¹ See, e.g., *King v. Burwell*, No. 14-1158 (4th Cir. July 22, 2014) (various provisions of the Affordable Care Act sufficiently indicate an expectation that tax credits will be available to participants in all health exchanges to cast doubt on whether provision specifically making credits available to participants in state exchanges implicitly denies credits to participants in federal exchanges).

²² Robert A. Katzman, *Judging Statutes* 31 (2016), at 10.

FDA for 7 or 11 years to treat the second disease or condition and in doing so, would provide meaningful incentives for continued rare disease drug development.

Considering the **Example 4**, CMS should clarify that – assuming the drug meets the other statutory requirements to become negotiation eligible as outlined in the IRA – the drug would become negotiation-eligible 7 or 11 years from the approval date for Disease O (i.e., in 2026 or 2030, 7 or 11 years from 2019).

Example 4: Orphan drug with multiple designations and multiple FDA-approved indications; CMS should clarify that the statutory period (i.e., 7 or 11 years) before negotiation starts at the approval that made the drug negotiation eligible (in this example 2026 or 2030, 7 or 11 years from 2019) – and not first approval (in this example 2021 or 2026, 7 or 11 years from 2014)

Drug 4 (multiple designations & multiple sequential FDA-approved indications)

Disease	Designation Year	FDA Approval Year
Rare Disease N	2011	2014
Rare Disease O	2016	2019
Rare Disease P	2016	-

For the reasons outlined above, NORD urges CMS to:

a. Clarify that if a drug has been designated under section 526 of the FFD&C Act for a second rare disease but has not been approved under section 505 (c) of the FFD&C Act or licensed under section 351(a) of the PHS for such disease, the drug will remain excluded from negotiation. As outlined above and illustrated in Examples 2 and 3, NORD believes this interpretation is consistent with the statute, maintaining Congressional intent to keep the orphan drug exclusion limited and will help protect the ODA incentives that have proven crucial for rare disease drug development.

b. Clarify that when a previously-excluded orphan drug becomes negotiation-eligible the statutory timeline for negotiation will begin from the time of the approval or licensure that made the drug negotiation-eligible, rather than from the very first approval or licensure in the drug’s regulatory history. As outlined above and illustrated in Example 4, this will provide regulatory predictability and ensure continued investments in orphan drug development so that rare disease patients can meaningfully benefit from the price negotiation process.

c. Continue to work closely with FDA on the implementation of the orphan drug exclusion. As outlined above, the negotiation program may impact orphan drug development and as a result FDA in a variety of ways; at the same time, CMS will base regulatory decisions on a history of FDA actions and databases that were not originally designed for these uses. Close alignment between the two agencies will be important to maximize the positive impacts of the negotiation program while minimizing unintended consequences.

4. Begin tracking the impact of the IRA on patient outcomes and innovation now to support a data-driven program evaluation

The IRA will impact patients and the larger healthcare ecosystem in complex and somewhat unpredictable ways; some of these impacts, such as greater affordability of life-altering therapies through out-of-pocket caps, will be unequivocally beneficial, while others, such as the impact on innovation, remain less clear. Some impacts on the healthcare ecosystem may begin long before the first negotiated price takes effect while others may not occur until many years later. Baseline data will be important to track and truly understand the impact of the drug negotiation program and to document its successes and challenges. Now is the time to ensure appropriate IT systems exist and robust data are collected and analyzed to evaluate these impacts today and for years and decades to come. In the rare disease space, data scarcity and limited populations available for study make tracking the impact of the IRA on orphan drugs even more challenging, requiring additional thought and attention be given to the tracking of intended and unintended consequences on rare disease patients.

NORD is concerned additional efforts are needed to meaningfully track IRA impacts on patient outcomes and the healthcare system. The IRA may impact the healthcare ecosystem in complex way. For instance, the new law may increase healthcare utilization and improve medication adherence because out-of-pocket costs are capped, possibly adding years to the life of impacted patients; physician prescribing behavior may be influenced by IRA-associated changes in reimbursement rates under Medicare Part B, with uncertain impacts on overall cost savings and patient costs and outcomes; changing incentives may impact the relative placement of negotiated drugs on formularies; and the healthcare ecosystem may be impacted in a many other ways, some we may not even anticipate, and possibly with wide-reaching ramifications beyond the patients directly utilizing the negotiated Medicare Part B and D drugs.

CMS has long taken a leadership role in developing and reporting quality measures that lead to better-quality healthcare and improved health outcomes through robust, consistent, and data-driven accountability.²³ Many of the lessons learned will be directly applicable and should inform IRA tracking efforts, including selecting metrics that are person-centered and meaningful to patients and caregivers; engaging stakeholders early and often in the measure development process; minimizing the burden associated with measurement; prioritizing outcome-based metrics where possible; and guarding against unintended consequences of measure implementation.²⁴ In addition, CMS processes for rigorously evaluating metrics against established criteria and gathering robust stakeholder feedback at every step of the measure lifecycle are some of the additional areas where quality measures can inform IRA tracking efforts.²⁵

NORD is also concerned additional efforts are needed to meaningfully track IRA impacts on innovation. Drug sponsors make decisions today that will impact the drug pipeline for decades to come. The IRA is likely to ultimately impact these decisions in a myriad of complex, interdependent, and hard-to-predict ways. NORD encourages CMS to work closely with FDA and other public and private-sector experts to establish meaningful metrics and monitor impacts on innovation. Tracking efforts will necessarily be limited by the available data systems and their ability to capture meaningful data, while many key data

²³ CMS: Quality Measures: How they are developed, used, & maintained; available at: <https://mmshub.cms.gov/sites/default/files/Guide-Quality-Measures-How-They-Are-Developed-Used-Maintained.pdf>; accessed 4/2023

²⁴ Ibid.

²⁵ Ibid.

sources to evaluate innovation in early research and development are proprietary and not readily available to the public. Moreover, consensus on appropriate metrics to capture pharmaceutical innovation during early research and development phases is largely lacking.²⁶ Given these challenges it appears likely that strategies to capture IRA impacts on pharmaceutical innovation will have to consider a relatively broad set of metrics in concert, looking at trends over time and across disease areas and geographic regions.

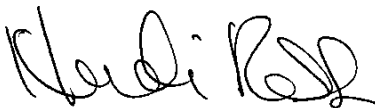
For the reasons outlined above, NORD urges CMS to:

a. Begin tracking key metrics to monitor and measure impacts on innovation and patient outcomes to ensure baseline data are available and as robust as possible. This will help lay a foundation for future evidence-based assessments of the IRA and draw thought and attention to the issue of data collection and tracking as well as help identify current key data gaps.

b. Engage with CMS quality metrics experts and other measurement experts within CMS, HHS, as well as government-wide and within the private and non-profit sector and issue requests for information (RFI) as applicable to reach agreement on what to measure and how to measure including key performance indicators (KPIs) and the data systems that generate the needed data. This will help lay the foundation for a resilient and sustainable tracking system to rigorously track and measure the impacts, intentional and unintentional, beneficial, and potentially harmful, of the IRA.

We thank CMS again for the opportunity to comment and look forward to working with CMS to ensure rare disease patients can fully participate in and benefit from the Negotiation Program. For questions related to this letter, please contact Heidi Ross, Vice President of Policy and Regulatory Affairs at HRoss@rarediseases.org or Karin Hoelzer, Director of Policy of Regulatory Affairs at KHoelzer@rarediseases.org

Sincerely,



Heidi Ross, MPH
Vice President, Policy and Regulatory Affairs,
National Organization for Rare Disorders



Karin Hoelzer, DVM, PhD
Director, Policy and Regulatory Affairs
National Organization for Rare Disorders

²⁶ Deshpande, A., Hood, C., Leach, B., Guthrie, S: Existing indicators to measure the biomedical innovation ecosystem; RAND 2019; available at: https://www.rand.org/content/dam/rand/pubs/working_papers/WR1300/WR1312/RAND_WR1312.pdf; accessed 4/2013



April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services
U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Meena Seshamani, M.D., Ph.D.
Deputy Administrator and Director of the Center
for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
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Dear Administrator Ms. Brooks-LaSure and Dr. Seshamani,

The 101 undersigned organizations, representing patients living with rare diseases and their families, thank you for the guidance released on March 15, 2023, specific to the Medicare Drug Price Negotiation

Program as required by the Inflation Reduction Act of 2022 (IRA). As the Centers for Medicare and Medicaid Services (CMS) continues to implement the provisions of this law, we urge you to further consider the unique perspective and challenges faced by rare disease patients and provide the following recommendations to ensure this law best serves the needs of the rare disease community.

As part of the IRA, and for the first time, CMS will negotiate the price of some prescription drugs available through the Medicare program. This will have significant impacts for some rare disease patients on their ability to afford needed treatments but could also impact broader rare disease drug development. For many of the more than 25 million Americans living with a rare disease, out of pocket prescription drug costs create significant financial barriers and hinder access to needed therapies. Key provisions in the IRA, including the \$2,000 annual and amortized monthly caps on out-of-pocket costs for Medicare Part D beneficiaries, ensure that more rare disease patients will be able to afford the life-altering therapies they need.

At the same time, the vast majority of the more than 7,000 known rare diseases do not have an FDA approved treatment. This makes continued research and innovation especially important to the rare disease community. Unfortunately, the small patient populations and medical complexity associated with rare diseases creates unique challenges to rare disease drug development. These same factors result in a scarcity of the data necessary to determine a fair negotiated price for products that treat rare diseases.

While CMS' most recent guidance includes several elements that positively impact the rare disease community, our organizations urge CMS to incorporate several changes into future guidance and program implementation to ensure the rare disease community fully benefits from the IRA.

Patient Engagement

We appreciate CMS' effort to incorporate the patient perspective into the negotiation program. Patients and caregivers have key insights on issues such as determining the value of a therapy and how it compares to potential alternate treatment options. For instance, rare disease patients are often uniquely positioned to share the challenges associated with unmet medical needs - when there are no or very few options available to treat their condition - and the benefits to themselves, their families and the community from a safe and effective therapy. Patient experience data will be particularly important given CMS' desire to evaluate price on an indication-specific level. We commend the agency for recognizing the unique value that drugs can bring to specific parts of the treated patient population, including patients that have few or no therapeutic alternatives.

In the rare disease community, published data to assess these specific uses remain scarce and patients and providers are often the best experts from which to elicit such information. While we are grateful CMS recognizes the value of patient experience data in the guidance we strongly encourage the agency to expand the opportunities available to patients to provide such input. We worry that the short timelines and limited proposed mechanisms for providing this input essentially make it impossible for patients to provide meaningful data. We urge CMS to 1) simplify and streamline the data submission process for patients and caregivers; 2) to clarify ahead of time what information the agency is seeking from patients and in what format to allow data standardization and aggregation, 3) to organize patient listening sessions specific to selected drugs to collect representative data while CMS is preparing the initial offer for a negotiated drug; and 4) include consistent and granular summaries of the data and assumptions on which each negotiation was based, including patient experience data.

Patient Access to Negotiated Drugs

We are supportive of the provision that requires negotiated products within the Medicare Part D program to be included on Part D plan formularies. However, we encourage CMS to take additional steps to ensure rare disease patients benefit from associated reduced out-of-pocket expenses and have timely access to negotiated products. Often, therapies that treat rare diseases are placed on the specialty tier of plan formularies, resulting in significant out-of-pocket costs and access delays for Medicare beneficiaries. Once a drug is negotiated it has been shown to be appropriately priced from CMS' perspective and should be placed on a higher formulary tier to reduce patient out-of-pocket costs.

Another common source of treatment delays or denials for our community are utilization management tools, such as prior authorization and/or step therapy. Health care providers, in partnership with their patients, are best positioned to choose the right therapy to treat the often-complex health care challenges faced by those with a rare disease. Given negotiated drugs will have been appropriately valued from CMS' perspective, we encourage CMS to require Medicare Part B and Medicare Part D plans to reduce or eliminate utilization management tools, including step therapy and/or prior authorization barriers to ensure patients are able to quickly access a negotiated drug.

Orphan Drug Exclusion

We acknowledge that the IRA includes a limited exclusion for orphan drugs that only treat one rare disease from drug price negotiation. However, we are concerned CMS' current interpretation of this rare disease exclusion, which makes products eligible for negotiation if they have been designated for two or more orphan diseases – even if the drug is not actually FDA approved to treat the second orphan disease - will disincentivize drug companies from conducting even the basic research necessary to develop a drug for additional rare diseases. Designating a drug for a rare disease is done very early on in the drug development process and does not allow the company to market the drug because it has not been proven to be safe and effective to treat that specific disease. We urge CMS to clarify that obtaining additional designations for a small molecule or biologic will not make a drug negotiation eligible until the drug has been approved by FDA to treat a second disease or condition.

From the rare disease patient community's perspective, successful IRA implementation hinges on a careful balance between greater affordability and maintaining appropriate incentives for continued investment in rare disease specific drug development. We thank CMS for the opportunity to comment on this latest IRA guidance and look forward to working with CMS to ensure rare disease patients and patient advocacy organizations can fully participate within this important effort and benefit from the law.

For questions related to this comment letter, please contact Heidi Ross, Vice President of Policy and Regulatory Affairs at the National Organization for Rare Disorders at HRoss@rarediseases.org.

Thank you for your consideration,

National Organization for Rare Disorders
A Cure in Sight
Alpha-1 Foundation
ALS Association
American Behcet's Disease Association
(ABDA)
American Partnership for Eosinophilic
Disorders

Angelman Syndrome Foundation
Autoimmune Encephalitis Alliance, Inc.
Avery's Hope
Bladder Cancer Advocacy Network (BCAN)
CancerCare
Children's PKU Network
Chondrosarcoma CS Foundation
Choroideremia Research Foundation

Chronic Disease Coalition
Coalition to Cure Calpain 3
Congenital Hyperinsulinism International
Consortium of MS Centers
Cure CMD
Cure HHT
Cure SMA
Cutaneous Lymphoma Foundation
Cystic Fibrosis Research Institute
DADA2 Foundation
Desmoid Tumor Research Foundation
Diann Shaddox Foundation for Essential
Tremor
Epilepsy Foundation
FACES: The National Craniofacial
Association
FD/MAS Alliance
Fibromuscular Dysplasia Society of America
FOD (Fatty Oxidation Disorders) Family
Support Group
Foundation for Sarcoidosis Research
Friedreich's Ataxia Research Alliance
(FARA)
Global Liver Institute
Gaucher Community Alliance
Global Healthy Living Foundation
Glut1 Deficiency Foundation
GRIN2B Foundation
Hepatitis B Foundation
Hydrocephalus Association
Hypertrophic Olivary Degeneration
Association
IgA Nephropathy Foundation
International Autoimmune Encephalitis
Society
International Foundation for Autoimmune &
Autoinflammatory Arthritis
International Pemphigus Pemphigoid
Foundation
International Waldenstrom's
Macroglobulinemia Foundation
KBG Foundation
Leukodystrophy Newborn Screening Action
Network
LGMD Awareness Foundation, Inc
Li-Fraumeni Syndrome Association (LFS
Association / LFSA)

LUNgevity Foundation
Lymphangiomatosis & Gorham's Disease
Alliance
MdDS Balance Disorder Foundation
MLD Foundation
Muscular Dystrophy Association
Myasthenia Gravis Foundation of America
Myocarditis Foundation
National Ataxia Foundation
National Bone Marrow Transplant Link
National MALS Foundation
National Oncology State Network
National PKU News
National Scleroderma Foundation
NBIA Disorders Association
NR2F1 Foundation
NTM Info & Research
Organic Acidemia Association
Phaware Global Association
Phelan-McDermid Syndrome Foundation
Project Alive
PWSA | USA
Reflex Sympathetic Dystrophy Syndrome
Association
RETpositive
SATB2 Gene Foundation
Spastic Paraplegia Foundation
SSADH Association
Super T's Mast Cell Foundation
Superficial Siderosis Research Alliance
Syngap 1 Foundation
TargetCancer Foundation
Tatton Brown Rahman Syndrome
Community
TEAM TELOMERE
Texas Prader Willi Association
The Akari Foundation
The Avalon Foundation
The Global Foundation for Peroxisomal
Disorders
The Jansen's Foundation
The Life Raft Group
The Mast Cell Disease Society
The Multiple System Atrophy Coalition
The RYR-1 Foundation
Thrive with Pyruvate Kinase Deficiency
Organization

United MSD Foundation
United Porphyrrias Association
Usher 1F Collaborative
Usher Syndrome Coalition
Usher Syndrome Society

Vasculitis Foundation
Vestibular Disorders Associations
wAIHA Warriors
Xia -Gibbs Society



April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
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Meena Seshamani, M.D., Ph.D.
Deputy Administrator and Director of the Center
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Dear Administrator Brooks-LaSure and Dr. Seshamani,

On behalf of the more than 25 million Americans living with one or more of the over 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) thanks the Centers for Medicare and Medicaid Services (CMS) for their extensive engagement with the rare disease community around implementation of the Inflation Reduction Act (IRA). NORD appreciates this opportunity to provide comments on the draft guidance ‘Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191- 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments,’ hereafter referred to as the “Negotiation Program” guidance.

NORD is a unique federation of non-profits and health organizations dedicated to improving the health and well-being of people living with rare diseases. NORD was founded 40 years ago, after the passage of the Orphan Drug Act (ODA), to formalize the coalition of patient advocacy groups that were instrumental in passing that landmark law. Our mission has always been and continues to be to improve the health and well-being of people with rare diseases by driving advances in care, research, and policy.

NORD appreciates CMS’ willingness in the Negotiation Program guidance (Section 30.1.1) to consider additional actions to “best support orphan drug development” and is pleased to submit these comments to help CMS make good on its commitment to the rare disease community. These comments are intended to supplement and expand on the April 14th comment letter submitted by NORD and 100 other patient advocacy organizations that support rare disease patients (available in the appendix).

For many Americans living with a rare disease, out of pocket prescription drug costs create significant financial barriers and hinder patient access to needed therapies. Key provisions in the IRA, including the \$2,000 annual and amortized monthly caps on out-of-pocket costs for Medicare Part D beneficiaries, as well as expanded eligibility for financial assistance for low-income beneficiaries, ensure that more rare disease patients on Medicare will be able to afford the life-altering therapies they need. Robust patient education, particularly about the opt-in requirement to the smoothing mechanism, will be critical to ensuring patients have access to and benefit from these provisions of the IRA. While outside the scope of this guidance, NORD would welcome the opportunity to partner with CMS to help educate the rare disease community as IRA-authorized benefits become available to Medicare beneficiaries at the appropriate time.

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As implemented under the draft guidance, however, the Negotiation Program may adversely impact rare disease drug development. Before the Orphan Drug Act was enacted in 1983, fewer than 40 Food and Drug Administration (FDA) approved therapies were available to treat rare diseases.¹ Thanks to the ODA, rare disease therapies now consistently account for more than half of FDA approvals for new molecular entities.² Still, more than 90% of the more than 7,000 known rare diseases do not have an FDA approved treatment, making continued investment in rare disease research and innovation critical to the rare disease community.³ The section 1192(e)(3) exclusion for orphan drugs approved to treat a single rare disease could help sustain this innovation, as will the broader exclusion for “low spend” drugs with less than \$200 million in annual Medicare spending. However, the small patient populations and medical complexity associated with rare diseases create unique challenges to drug development. These small population sizes and complex, heterogenous disease manifestations also result in a more limited availability of data on issues such as clinical benefit and therapeutic alternatives, making it more difficult to determine a fair negotiated price for drugs that treat rare diseases compared to other therapies. Therefore, NORD appreciates the opportunity to highlight additional ways that CMS, consistent with the statute, can further support rare disease drug development in implementing the Negotiation Program.

Successful Negotiation Program implementation hinges on a careful balance between greater affordability and maintaining appropriate incentives for continued rare disease drug development. NORD urges CMS to address four areas of concern in future guidance:

1. Actively engage patients and create opportunities to provide meaningful data and insights;
2. Ensure rare disease patients have access to the negotiated therapies;
3. Further clarify the scope and timing of the orphan drug exclusion; and
4. Begin tracking the impact of the IRA on innovation and patient outcomes now.

Specifically, CMS should take the following steps to support rare disease patients and families:

1. Expand and strengthen data collection and engagement opportunities to ensure patients can meaningfully contribute their unique insights on the negotiated drug and its alternatives.

NORD commends CMS’ efforts to consider data on clinical benefit, therapeutic alternatives, and unmet medical need in the negotiation process and to incorporate relevant patient and provider perspectives. NORD thanks CMS for recognizing, in section 60 of the draft guidance, the unique and nuanced value orphan drugs can bring to specific subsets of the patient population, including those with few or no therapeutic alternatives. The agency’s stated objective to assess value in an indication-specific manner, including some off-label uses, is critical for CMS to fully understand and account for the complex treatment trade-offs and unmet needs that exist within the rare disease patient community.

Moreover, we are encouraged that the draft guidance explicitly recognizes the value of patient experience data, including its nuances, in section 60.3.3, and that not all patients are necessarily sharing the same

¹ Orphan Drugs In The United States: An Examination of Patents and Orphan Drug Exclusivity (2021): available at https://rarediseases.org/wp-content/uploads/2022/10/NORD-Avalere-Report-2021_FNL-1.pdf; accessed 4/2023

² New Drugs at FDA: CDER’s New Molecular Entities and New Therapeutic Biological Products; available at: <https://www.fda.gov/drugs/development-approval-process-drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products>; accessed 4/2023

³ Larkindale J, Betourne A, Borens A, Boulanger V, Theurer Crider V, Gavin P, Burton J, Liwski R, Romero K, Walls R, Barrett JS. Innovations in Therapy Development for Rare Diseases Through the Rare Disease Cures Accelerator-Data and Analytics Platform. *Ther Innov Regul Sci*. 2022 Sep;56(5):768-776. doi: 10.1007/s43441-022-00408-x.

views and experiences. For instance, the science of patient engagement has long recognized that patient experience data may reflect differences depending on disease progression or a patient's cultural, geographic, and socio-economic background. While we are grateful CMS recognizes the value of patient experience data, we strongly encourage CMS to expand the opportunities and strengthen the processes for providing such input to the agency as part of the negotiation process.

NORD is concerned that CMS' proposed approach would make it essentially impossible for patients and providers to submit meaningful data. CMS plans to largely rely on voluntary, public data submissions, on very short timelines, without meaningful data standardization, using complicated forms written at too-advanced reading levels and through hard-to-navigate processes that are neither intuitive nor patient-friendly. Patients will either not become aware of data collection efforts in time, or struggle to navigate the complex submission process. In addition, the required attestations are worded in a way that will likely discourage many patients from submitting data. To the extent patients will feel compelled to submit data containing Personal Identifiable Information (PII) and Personal Health Information (PHI), the data collection also raises privacy concerns.

Moreover, NORD foresees challenges in aggregating and analyzing individual patient and provider experience data submitted through this process. The data will be collected without a sampling frame and likely not representative while the collection method essentially makes it impossible to determine or account for such inherent biases in the data. In addition, the lack of standardized questions and scientific rigor will likely render this data largely anecdotal. This would contrast sharply with appropriate qualitative and/or quantitative research methodologies that would collect information in a scientifically rigorous and reproducible manner. A good example of such rigorous approaches is data collected through the FDA's patient-focused drug development (PFDD) meetings or patient surveys. Specifically, FDA's "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input" guidance⁴ provides detailed and tangible advice on operationalizing and standardizing data collection and data management in ways that are feasible for the rare disease patient community.

CMS will have to refine its proposed approach to incorporate meaningful external data sources. CMS plans to supplement the aforementioned data submitted by the public with relevant published data retrievable through literature searches. Unfortunately, for many rare diseases, data relevant to determine a negotiated drug's clinical benefit, therapeutic alternatives, or unmet medical need does not currently exist in peer-reviewed journals or consensus treatment guidelines. Additionally, the lack of disease-specific International Classification of Disease (ICD-10) codes for most rare diseases makes Real-World Data (RWD) sources such as Electronic Health Records (EHRs) or medical claims data largely infeasible for many rare diseases. This is a recognized challenge within rare diseases.

FDA's Voice of the Patient (VOIP) reports are designed to address this data scarcity and are critical to patient-focused drug development by assembling meaningful information on how patients evaluate therapeutic alternatives or characterize the unmet need and clinical benefit of alternatives. However, these data are not indexed in a way that would clearly find them in a traditional literature search. CMS should consider all relevant data collected as part of the FDA approval process in the negotiation process. Moreover, patient and provider engagement will be critical to ensure CMS is aware of and able to leverage all other available and relevant data sources regardless of how they are indexed.

⁴ FDA GFI: Patient-Focused Drug Development: Collecting Comprehensive and Representative Input; available at <https://www.fda.gov/media/139088/download>; accessed 4/2023

CMS will consequently have to collect data on treatment alternatives, clinical benefits, and unmet medical need for rare diseases *de novo*, including from patients, caregivers, and providers. Patients and caregivers have key insights on issues such as determining the value of a therapy and how it compares to potential alternate treatment options. Rare disease patients are often uniquely positioned to share the challenges associated with unmet medical needs - when there are no or very few options available to treat their condition - and the benefits to themselves, their families, and the community from a safe and effective therapy. Patient experience data will be particularly important given CMS' desire to evaluate drug prices on an indication-specific level including certain off-label uses, which are common in the rare disease space albeit notoriously hard to study.⁵ Because published data to assess these specific uses remain scarce, patients and providers are often the best experts from which to elicit such information related to rare disease treatments.

For the reasons outlined above, NORD urges CMS to:

a. Simplify and streamline the data submission process for patients, caregivers, and providers to eliminate barriers to their providing the requested information. This should include pre-testing the forms, attestations, and instructions with representatives of the relevant community to ensure they are clearly understood and easy to navigate, including by individuals with visual and other impairments. Because this data submission is voluntary and not subject to the 30-day statutory data submission timeline for mandatory manufacturer-provided data, CMS should work with the patient community to establish feasible timelines that will be workable for the community. FDA listening sessions, PFDD meetings, and other FDA-led initiatives routinely collect meaningful patient experience data in ways that works for rare disease patients and families and can serve as another valuable guide and resource for CMS, including all applicable attestations and data protections.

b. Clarify what information the agency is seeking from patients to allow data standardization and aggregation. The short time for submitting data makes it imperative to provide detailed instructions as early as possible, before the negotiation period begins, to facilitate and streamline the collection and submission of meaningful data. Clarifying the key data elements ahead of time will also empower patient advocacy groups and other important stakeholders to proactively collect and collate relevant information in a way that is scientifically rigorous and representative of the relevant patient community.

c. Organize CMS-led patient listening sessions specific to selected drugs to collect representative data within the different drug indications to inform CMS' initial offer for a negotiated drug. In planning for these sessions, CMS should use FDA patient listening sessions as a roadmap and work closely with the various impacted patient communities to develop a representative and meaningful data collection effort. For instance, while we appreciate why CMS intends to only focus on pharmaceutical alternatives and to primarily consider alternatives in the same drug class, we recognize non-pharmaceutical options such as surgery are often the only viable alternative for our patient populations and that therapeutic alternatives in other drug classes and with other mechanisms of actions may in fact be the most appropriate alternatives for some of our patients. Engaging the patient community in planning the listening sessions will help ensure that these alternatives are appropriately considered. Close collaboration with FDA will enable CMS to benefit from FDA's relevant best practices and extensive experience.

⁵ Fung A, Yue X, Wigle PR, Guo JJ. Off-label medication use in rare pediatric diseases in the United States. *Intractable Rare Dis Res.* 2021 Nov;10(4):238-245. doi: 10.5582/irdr.2021.01104. PMID: 34877235; PMCID: PMC8630459.

d. Include consistent and granular summaries of the data and assumptions on which each negotiation was based, including patient experience data. We urge CMS to report a detailed and standardized summary of the data relied upon in the negotiation process including the therapeutic alternatives, clinical benefit, off-label use, and unmet need for each indication and the data sources relied upon. CMS should further break out the use of patient experience data and patient-reported outcomes; list data identified by CMS through literature searches and guideline review; and identify primary data, such as claims, electronic health record (EHR), or other real-world-evidence, generated and collated by CMS. This level of transparency will be important to create consistency and trust in the negotiation process. Clearly breaking out the use of different data sources will also motivate the creation of valuable data sources including patient experience data for future negotiation years. In fact, much of the data for rare diseases collected through this process will be unique and have value beyond this specific negotiation process.

2. Give negotiated drugs a preferred place on the formulary and minimize utilization burdens to ensure patients have ready access to the negotiated drugs.

NORD supports section 1860D-4(b)(3)(I) of the Social Security Act which will require Medicare Part D negotiated drugs to be included on Part D plan formularies. However, we encourage CMS to take additional steps to ensure rare disease patients benefit from reduced out-of-pocket expenses associated with better formulary tier placement and to better assure their timely access to negotiated drugs through reduced utilization management processes.

Often, rare disease drugs are placed on the non-preferred or specialty tiers of Medicare Part D plan formularies, resulting in significant out-of-pocket costs and access delays. For instance, a study published in the *American Journal of Managed Care* (AJMC) in 2020 found “on average, 85% of orphan drugs on a [Medicare Part D] formulary were placed on its highest cost-sharing tier.”⁶ Similarly, a KFF analysis of 2023 Medicare Part D plans found that in 12 of the 16 the national prescription drug plans, coinsurance amounts for non-preferred drugs range from 40% to 50%, showing similar trends as in previous plan years.⁷ Moreover, 44% of these plans’ enrollees will face coinsurance ranging from 15% to 25% for preferred brands⁸, meaning less predictable and often higher out of pocket costs for patients compared to flat copays. KFF also found that the median coinsurance for drugs on the specialty tier was 25%.⁹

Another common source of treatment delays or denials for rare disease patients is related to prior authorization and step therapy. NORD believes health care providers, in partnership with their patients, are best positioned to choose the right therapy to treat the often-complex health care challenges faced by those with a rare disease. Yet, a 2020 study found that a staggering 76% of orphan drugs on Medicare Part D formularies were subject to prior authorization.¹⁰ Similarly, a 2021 study¹¹ found that nearly 40

⁶ Yehia, F., Segal, J.B. Predictors of Orphan Drug Coverage Restrictions in Medicare Part D. 2020 Sep; AJMC 26(09); accessible at <https://www.ajmc.com/view/predictors-of-orphan-drug-coverage-restrictions-in-medicare-part-d>

⁷ Kaiser Family Foundation (KFF): Medicare Part D: A First Look at Medicare Drug Plans in 2023; available at: <https://www.kff.org/medicare/issue-brief/medicare-part-d-a-first-look-at-medicare-drug-plans-in-2023/>; accessed 4/2023

⁸ Kaiser Family Foundation (KFF): Medicare Part D: A First Look at Medicare Drug Plans in 2023; available at: <https://www.kff.org/medicare/issue-brief/medicare-part-d-a-first-look-at-medicare-drug-plans-in-2023/>; accessed 4/2023

⁹ Ibid.

¹⁰ Yehia, F., Segal, J.B. Predictors of Orphan Drug Coverage Restrictions in Medicare Part D. 2020 Sep; AJMC 26(09); accessible at <https://www.ajmc.com/view/predictors-of-orphan-drug-coverage-restrictions-in-medicare-part-d>

¹¹ Lenahan, K.L., Nichols, D.E., Gertler, R.M., Chambers, J.D.: Variations in Use and Content of Prescription Drug Step Therapy Protocols, Within and Across health Plans. 2021, Nov; Health Affairs 40(11); <https://doi.org/10.1377/hlthaff.2021.00822>; available at <https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2021.00822>

percent of the specialty drugs offered within the 17 largest commercial health plans included step therapy in the drug coverage plan. Additionally, 55.6 percent of the step therapy protocols were found to be more stringent than clinical guidelines,¹² delaying timely patient access to appropriate care.¹³

From CMS' perspective, negotiated drugs will have been appropriately valued and therefore, we encourage CMS to:

a. Require that a negotiated drug be placed on a higher formulary tier to improve patient access through further reduced patient out-of-pocket costs. While the \$2,000 annual out-of-pocket cap and the smoothing mechanism to spread a patient's out-of-pocket costs out over the plan year will be tremendously helpful to Medicare patients living with a rare disease, coinsurance makes it more difficult for patients to predict their out-of-pocket expenditures. Requiring a negotiated drug's placement on formulary tiers that typically have copays instead of coinsurance can assist patients with both planning for prescription drug expenses and their ability to pay for their medications at the time they need them.

b. Significantly reduce or eliminate step therapy and prior authorization barriers in Medicare Part B and Medicare Part D for negotiated drugs. To further ensure timely access to these drugs, NORD urges CMS to include utilization management protections for negotiated drugs that have been determined by CMS to be appropriately priced. In the 2024 Medicare Advantage and Part D Final Rule (CMS-4201-F) released on April 5, 2023, and effective for the CY 2024 plan year, CMS will require "an approval granted through prior authorization processes must be valid for as long as medically necessary to avoid disruptions in care in accordance with applicable coverage criteria, the patient's medical history, and the treating provider's recommendation, and that plans provide a minimum 90-day transition period when an enrollee who is currently undergoing an active course of treatment switches to a new MA plan."¹⁴ NORD encourages the adoption of these or similar requirements for negotiated drugs offered on traditional Medicare Part D plan formularies as well.

3. Ensure CMS' interpretation of the orphan drug exclusion protects vital incentives for rare disease drug development

While the IRA includes a limited exclusion for orphan drugs that only treat one rare disease from drug price negotiation, NORD is greatly concerned with the potential impact of CMS' proposed interpretation of the exclusion on future innovation in rare disease drug development. Today, about 60 percent of all orphan drugs have a single FDA-approved indication, whereas only about 20 percent are FDA-approved for both orphan and non-orphan indications.¹⁵ Among the drugs that only have orphan indications, fewer than a quarter have more than one FDA-approved indication and fewer than 10 percent have three or more approved indications.¹⁶ Similarly, among the drugs that have both orphan and non-orphan indications, less than 20 percent have 3 or more orphan indications. This indicates that to date, relatively few orphan drugs have been successfully developed for more than one disease.

¹² Ibid.

¹³ Ibid.

¹⁴ Centers for Medicare & Medicaid Services (CMS); RIN 0938-AU96 Medicare Program; Contract Year 2024 Policy and Technical Changes to the Medicare Advantage Program, Medicare Prescription Drug Benefit Program, Medicare Cost Plan Program, and Programs of All-Inclusive Care for the Elderly; available at <https://public-inspection.federalregister.gov/2023-07115.pdf>; accessed 4/2023

¹⁵ IQVIA: Orphan Drugs in the United States. 2020; Dec; available at: <https://rarediseases.org/wp-content/uploads/2022/10/orphan-drugs-in-the-united-states-NRD-2020.pdf>; accessed 4/2023

¹⁶ Ibid.

Still, developing already-approved therapies to treat additional rare diseases is a critical strategy to address the rare disease community's significant unmet need because these drugs have already proven to be safe for humans. In fact, according to a recent analysis, over 3,000 unique drugs have been FDA-designated as rare disease drugs and studied, with about a quarter of these drugs being designated for more than one rare disease.¹⁷ Serial innovation and the investigation and development of multiple rare disease indications of use is an increasingly important dimension of orphan drug development, making the preservation of incentives to further develop drugs to treat additional orphan diseases after they have entered the market particularly important.

NORD also recognizes that relatively few orphan-only drugs will meet the annual revenue threshold of \$200,000,000 in combined expenditures under Medicare Parts B and D to make a drug negotiation-eligible. However, due to the complexity and long timeline from initial drug discovery and early research and development to FDA approval, drug sponsors are making decisions today that will impact their investments and drug development pipeline for decades to come. Remaining uncertainty about if, when, and how rare disease drugs will become negotiation eligible creates real business risks that work as strong disincentives to develop drugs for the limited populations impacted by rare diseases. Therefore, as part of the negotiation process, NORD urges CMS to make clear that research and development efforts in support of innovative therapies that help address unmet needs will be treated favorably in the price negotiation process.

We thank CMS for clarifying in the draft guidance that an orphan drug with multiple FDA-approved indications within the scope of an orphan drug designation for one rare disease (i.e., multiple indications tied to one orphan designation as shown in **Example 1**) remains excluded from negotiation. As a result, drug sponsors will consequently not be discouraged or penalized for further developing a rare disease drug for new sub-populations, such as children, or specific disease subtypes.

Example 1 - Orphan drug with one designation & multiple associated approved indications; CMS already clarified this is excluded from negotiation; this example was selected to be illustrative while reflecting common trends in orphan drug approvals.

Drug 1 (one designation, multiple FDA-approved indications)			
Designations		FDA Approved Indications	
Disease	Year	Year	Population
Rare Disease A	2014	2015	12 years and older
		2016	6 years and older
		1018	2 years and older
		2022	1 year and older

However, NORD is gravely concerned that CMS' interpretation of the orphan drug exclusion might contravene the intent of the ODA by discouraging drug sponsors from developing their drug for additional rare diseases. Specifically, CMS' interpretation of the IRA makes drugs eligible for negotiation as soon as they have been designated under section 526 of the Federal Food, Drug, and Cosmetic Act

¹⁷ Miller, KL, Kraft, S, Ipe, A, and Fermaglich, L. Drugs and biologics receiving FDA orphan drug designation: an analysis of the most frequently designated products and their repositioning strategies. Expert Opin Orphan Drugs. 2022 Mar 1;9(11-12):265-272. doi: 10.1080/21678707.2021.2047021.

(FFD&C) for more than one orphan disease – even if the drug is not actually FDA approved (or indicated) to treat more than one of the designated orphan diseases. For instance, consider **Example 2** and the many other rare disease drugs with similar regulatory history; although this drug has been designated for five different rare diseases, it is only FDA approved to treat a single orphan disease.

Example 2: Orphan drug with multiple designations and one FDA-approved indication; CMS should clarify that that this drug will be excluded from negotiation because while it has five designations, it only has one approved indication.

Drug 2 (multiple designations, one FDA-approved indication)

Disease	Designation Year	FDA Approval Year
Rare Disease B	2007	2017
Rare Disease C	2009	-
Rare Disease D	2016	-
Rare Disease E	2018	-
Rare Disease F	2019	-

Designating an orphan drug under section 526 of the FFD&C Act is done early in the drug development process and much earlier than submission of a New Drug Application (NDA) or Biological License Application (BLA). Orphan drug designation is critical to access to ODA incentives such as funding and tax credits for clinical research to help de-risk this phase of drug development. However, an orphan drug designation does not allow the company to market the drug; it is only the first in many steps towards approval and marketing. In fact, FDA’s Orphan Drug Designations and Approvals database currently contains 6,445 orphan drug designations (including withdrawn designations) compared to only 1130 approved orphan indications, demonstrating that a vast majority of orphan drug designations do not result in any FDA-approved indications – and therefore are largely irrelevant to the pricing considerations central to the Negotiation Program.¹⁸

NORD understands that the language of section 1192(e)(3), due to the manner in which it was drafted, is ambiguous and therefore open to CMS interpretation. CMS states that to qualify for the orphan drug exclusion, “the drug or biological drug must (1) be designated as a drug for only one rare disease or condition under section 526 of the FFD&C Act and (2) be approved by the FDA for only one or more indications within such designated rare disease or condition.”¹⁹ This two-prong test, embodying two separate and distinct criteria, is a possible interpretation of the statute. But under the canons of legislative drafting, if the congressional authors had intended the two clauses to be read *independently*, the proper legislative drafting would have structured the two clauses separately and in sequence. Instead, Congress did not separate the clauses, intending them to be read *together*: that a drug designated for a given “rare disease or condition” has “only [one] approved indication” or multiple “approved... indications” *within the scope of that designation*. CMS substantiates this plain meaning²⁰ of the provision in accepting that

¹⁸ US FDA Orphan Drug Designations and Approvals database; available at <https://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm>; accessed 4/2023

¹⁹ Meena Seshamani, Memorandum to Interested Parties: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments, March 15, 2023, at 10-11.

²⁰ E.g., *Sebelius v. Cloer*, 569 U.S. ___, No. 12-236, slip op. (May 20, 2013).

an orphan drug with **multiple** (“one or more”) FDA-approved indications qualifies for the exclusion provided all such approved indications are within the scope of a **single** (“only one”) **designation**.

A two-prong test also does not best reflect and advance the purposes and function of the Negotiation Program. The cardinal rule of statutory construction is that the whole statute should be drawn upon as necessary, with its various parts being interpreted within their broader statutory context in a manner that furthers statutory purposes.²¹ The proper interpretation of the orphan drug exclusion “in a manner consistent with [the] legislative purposes”²² of the Negotiation Program preserves an intentionally narrow class of qualifying orphan drugs determined upon the basis of a drug’s FDA **approval history** – not on orphan drug designations which have no bearing on, or applicability to, prescription drug marketing or pricing.

In considering the regulatory history for the drug shown in **Example 3**, the approval for Disease H in 2014 should trigger the drug becoming negotiation eligible (assuming it meets the other statutory requirements outlined in the IRA), rather than the Designation for Diseases H or I in 2010, thus preserving vital rare disease research and development incentives. One of the critical “additional actions” that CMS can take to support rare disease research and development would be to revise its guidance to reflect a sound statutory interpretation more fully in line with congressional intent to make an orphan drug negotiation eligible once it has been approved (or indicated) to treat a second disease.

Example 3: Orphan drug with multiple designations and multiple FDA-approved indications; CMS should clarify that an orphan drug with multiple designations and approved indications becomes negotiation eligible when the drug is approved for the second disease (in this example 2014) – NOT upon second designation in 2010.

Drug 3 (multiple designations & multiple FDA-approved indications)

Disease	Designation Year	FDA Approval Year
Rare Disease G	2008	2011
Rare Disease H	2010	2014
Rare Disease I	2010	-
Rare Disease J	2013	-

NORD is also concerned about the potential chilling effect residual uncertainty about CMS’s implementation of the orphan drug exclusion will have on rare disease drug development. CMS remains silent as to when orphan drugs that receive FDA approval for a second disease and therefore lose eligibility for the orphan drug exclusion would become negotiation eligible. Qualifying single-source drugs must have been approved at least 7 years and qualifying single-source biologics must have been licensed at least 11 years to qualify, but CMS has not yet clarified if the 7 or 11 years will be counted beginning on the date of the FDA approval for the second disease that made the drug negotiation eligible or based on the first orphan drug approval. CMS should clarify that obtaining additional designations for a small molecule or biologic will not make a drug negotiation eligible until the drug has been approved by

²¹ See, e.g., *King v. Burwell*, No. 14-1158 (4th Cir. July 22, 2014) (various provisions of the Affordable Care Act sufficiently indicate an expectation that tax credits will be available to participants in all health exchanges to cast doubt on whether provision specifically making credits available to participants in state exchanges implicitly denies credits to participants in federal exchanges).

²² Robert A. Katzman, *Judging Statutes* 31 (2016), at 10.

FDA for 7 or 11 years to treat the second disease or condition and in doing so, would provide meaningful incentives for continued rare disease drug development.

Considering the **Example 4**, CMS should clarify that – assuming the drug meets the other statutory requirements to become negotiation eligible as outlined in the IRA – the drug would become negotiation-eligible 7 or 11 years from the approval date for Disease O (i.e., in 2026 or 2030, 7 or 11 years from 2019).

Example 4: Orphan drug with multiple designations and multiple FDA-approved indications; CMS should clarify that the statutory period (i.e., 7 or 11 years) before negotiation starts at the approval that made the drug negotiation eligible (in this example 2026 or 2030, 7 or 11 years from 2019) – and not first approval (in this example 2021 or 2026, 7 or 11 years from 2014)

Drug 4 (multiple designations & multiple sequential FDA-approved indications)

Disease	Designation Year	FDA Approval Year
Rare Disease N	2011	2014
Rare Disease O	2016	2019
Rare Disease P	2016	-

For the reasons outlined above, NORD urges CMS to:

a. Clarify that if a drug has been designated under section 526 of the FFD&C Act for a second rare disease but has not been approved under section 505 (c) of the FFD&C Act or licensed under section 351(a) of the PHS for such disease, the drug will remain excluded from negotiation. As outlined above and illustrated in Examples 2 and 3, NORD believes this interpretation is consistent with the statute, maintaining Congressional intent to keep the orphan drug exclusion limited and will help protect the ODA incentives that have proven crucial for rare disease drug development.

b. Clarify that when a previously-excluded orphan drug becomes negotiation-eligible the statutory timeline for negotiation will begin from the time of the approval or licensure that made the drug negotiation-eligible, rather than from the very first approval or licensure in the drug's regulatory history. As outlined above and illustrated in Example 4, this will provide regulatory predictability and ensure continued investments in orphan drug development so that rare disease patients can meaningfully benefit from the price negotiation process.

c. Continue to work closely with FDA on the implementation of the orphan drug exclusion. As outlined above, the negotiation program may impact orphan drug development and as a result FDA in a variety of ways; at the same time, CMS will base regulatory decisions on a history of FDA actions and databases that were not originally designed for these uses. Close alignment between the two agencies will be important to maximize the positive impacts of the negotiation program while minimizing unintended consequences.

4. Begin tracking the impact of the IRA on patient outcomes and innovation now to support a data-driven program evaluation

The IRA will impact patients and the larger healthcare ecosystem in complex and somewhat unpredictable ways; some of these impacts, such as greater affordability of life-altering therapies through out-of-pocket caps, will be unequivocally beneficial, while others, such as the impact on innovation, remain less clear. Some impacts on the healthcare ecosystem may begin long before the first negotiated price takes effect while others may not occur until many years later. Baseline data will be important to track and truly understand the impact of the drug negotiation program and to document its successes and challenges. Now is the time to ensure appropriate IT systems exist and robust data are collected and analyzed to evaluate these impacts today and for years and decades to come. In the rare disease space, data scarcity and limited populations available for study make tracking the impact of the IRA on orphan drugs even more challenging, requiring additional thought and attention be given to the tracking of intended and unintended consequences on rare disease patients.

NORD is concerned additional efforts are needed to meaningfully track IRA impacts on patient outcomes and the healthcare system. The IRA may impact the healthcare ecosystem in complex way. For instance, the new law may increase healthcare utilization and improve medication adherence because out-of-pocket costs are capped, possibly adding years to the life of impacted patients; physician prescribing behavior may be influenced by IRA-associated changes in reimbursement rates under Medicare Part B, with uncertain impacts on overall cost savings and patient costs and outcomes; changing incentives may impact the relative placement of negotiated drugs on formularies; and the healthcare ecosystem may be impacted in a many other ways, some we may not even anticipate, and possibly with wide-reaching ramifications beyond the patients directly utilizing the negotiated Medicare Part B and D drugs.

CMS has long taken a leadership role in developing and reporting quality measures that lead to better-quality healthcare and improved health outcomes through robust, consistent, and data-driven accountability.²³ Many of the lessons learned will be directly applicable and should inform IRA tracking efforts, including selecting metrics that are person-centered and meaningful to patients and caregivers; engaging stakeholders early and often in the measure development process; minimizing the burden associated with measurement; prioritizing outcome-based metrics where possible; and guarding against unintended consequences of measure implementation.²⁴ In addition, CMS processes for rigorously evaluating metrics against established criteria and gathering robust stakeholder feedback at every step of the measure lifecycle are some of the additional areas where quality measures can inform IRA tracking efforts.²⁵

NORD is also concerned additional efforts are needed to meaningfully track IRA impacts on innovation. Drug sponsors make decisions today that will impact the drug pipeline for decades to come. The IRA is likely to ultimately impact these decisions in a myriad of complex, interdependent, and hard-to-predict ways. NORD encourages CMS to work closely with FDA and other public and private-sector experts to establish meaningful metrics and monitor impacts on innovation. Tracking efforts will necessarily be limited by the available data systems and their ability to capture meaningful data, while many key data

²³ CMS: Quality Measures: How they are developed, used, & maintained; available at: <https://mmshub.cms.gov/sites/default/files/Guide-Quality-Measures-How-They-Are-Developed-Used-Maintained.pdf>; accessed 4/2023

²⁴ Ibid.

²⁵ Ibid.

sources to evaluate innovation in early research and development are proprietary and not readily available to the public. Moreover, consensus on appropriate metrics to capture pharmaceutical innovation during early research and development phases is largely lacking.²⁶ Given these challenges it appears likely that strategies to capture IRA impacts on pharmaceutical innovation will have to consider a relatively broad set of metrics in concert, looking at trends over time and across disease areas and geographic regions.

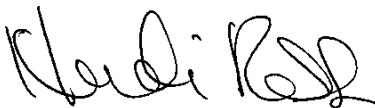
For the reasons outlined above, NORD urges CMS to:

a. Begin tracking key metrics to monitor and measure impacts on innovation and patient outcomes to ensure baseline data are available and as robust as possible. This will help lay a foundation for future evidence-based assessments of the IRA and draw thought and attention to the issue of data collection and tracking as well as help identify current key data gaps.

b. Engage with CMS quality metrics experts and other measurement experts within CMS, HHS, as well as government-wide and within the private and non-profit sector and issue requests for information (RFI) as applicable to reach agreement on what to measure and how to measure including key performance indicators (KPIs) and the data systems that generate the needed data. This will help lay the foundation for a resilient and sustainable tracking system to rigorously track and measure the impacts, intentional and unintentional, beneficial, and potentially harmful, of the IRA.

We thank CMS again for the opportunity to comment and look forward to working with CMS to ensure rare disease patients can fully participate in and benefit from the Negotiation Program. For questions related to this letter, please contact Heidi Ross, Vice President of Policy and Regulatory Affairs at HRoss@rarediseases.org or Karin Hoelzer, Director of Policy of Regulatory Affairs at KHoelzer@rarediseases.org

Sincerely,



Heidi Ross, MPH
Vice President, Policy and Regulatory Affairs,
National Organization for Rare Disorders



Karin Hoelzer, DVM, PhD
Director, Policy and Regulatory Affairs
National Organization for Rare Disorders

²⁶ Deshpande, A., Hood, C., Leach, B., Guthrie, S: Existing indicators to measure the biomedical innovation ecosystem; RAND 2019; available at: https://www.rand.org/content/dam/rand/pubs/working_papers/WR1300/WR1312/RAND_WR1312.pdf; accessed 4/2013



April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services
U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Meena Seshamani, M.D., Ph.D.
Deputy Administrator and Director of the Center
for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Dear Administrator Ms. Brooks-LaSure and Dr. Seshamani,

The 101 undersigned organizations, representing patients living with rare diseases and their families,
thank you for the guidance released on March 15, 2023, specific to the Medicare Drug Price Negotiation

Program as required by the Inflation Reduction Act of 2022 (IRA). As the Centers for Medicare and Medicaid Services (CMS) continues to implement the provisions of this law, we urge you to further consider the unique perspective and challenges faced by rare disease patients and provide the following recommendations to ensure this law best serves the needs of the rare disease community.

As part of the IRA, and for the first time, CMS will negotiate the price of some prescription drugs available through the Medicare program. This will have significant impacts for some rare disease patients on their ability to afford needed treatments but could also impact broader rare disease drug development. For many of the more than 25 million Americans living with a rare disease, out of pocket prescription drug costs create significant financial barriers and hinder access to needed therapies. Key provisions in the IRA, including the \$2,000 annual and amortized monthly caps on out-of-pocket costs for Medicare Part D beneficiaries, ensure that more rare disease patients will be able to afford the life-altering therapies they need.

At the same time, the vast majority of the more than 7,000 known rare diseases do not have an FDA approved treatment. This makes continued research and innovation especially important to the rare disease community. Unfortunately, the small patient populations and medical complexity associated with rare diseases creates unique challenges to rare disease drug development. These same factors result in a scarcity of the data necessary to determine a fair negotiated price for products that treat rare diseases.

While CMS' most recent guidance includes several elements that positively impact the rare disease community, our organizations urge CMS to incorporate several changes into future guidance and program implementation to ensure the rare disease community fully benefits from the IRA.

Patient Engagement

We appreciate CMS' effort to incorporate the patient perspective into the negotiation program. Patients and caregivers have key insights on issues such as determining the value of a therapy and how it compares to potential alternate treatment options. For instance, rare disease patients are often uniquely positioned to share the challenges associated with unmet medical needs - when there are no or very few options available to treat their condition - and the benefits to themselves, their families and the community from a safe and effective therapy. Patient experience data will be particularly important given CMS' desire to evaluate price on an indication-specific level. We commend the agency for recognizing the unique value that drugs can bring to specific parts of the treated patient population, including patients that have few or no therapeutic alternatives.

In the rare disease community, published data to assess these specific uses remain scarce and patients and providers are often the best experts from which to elicit such information. While we are grateful CMS recognizes the value of patient experience data in the guidance we strongly encourage the agency to expand the opportunities available to patients to provide such input. We worry that the short timelines and limited proposed mechanisms for providing this input essentially make it impossible for patients to provide meaningful data. We urge CMS to 1) simplify and streamline the data submission process for patients and caregivers; 2) to clarify ahead of time what information the agency is seeking from patients and in what format to allow data standardization and aggregation, 3) to organize patient listening sessions specific to selected drugs to collect representative data while CMS is preparing the initial offer for a negotiated drug; and 4) include consistent and granular summaries of the data and assumptions on which each negotiation was based, including patient experience data.

Patient Access to Negotiated Drugs

We are supportive of the provision that requires negotiated products within the Medicare Part D program to be included on Part D plan formularies. However, we encourage CMS to take additional steps to ensure rare disease patients benefit from associated reduced out-of-pocket expenses and have timely access to negotiated products. Often, therapies that treat rare diseases are placed on the specialty tier of plan formularies, resulting in significant out-of-pocket costs and access delays for Medicare beneficiaries. Once a drug is negotiated it has been shown to be appropriately priced from CMS' perspective and should be placed on a higher formulary tier to reduce patient out-of-pocket costs.

Another common source of treatment delays or denials for our community are utilization management tools, such as prior authorization and/or step therapy. Health care providers, in partnership with their patients, are best positioned to choose the right therapy to treat the often-complex health care challenges faced by those with a rare disease. Given negotiated drugs will have been appropriately valued from CMS' perspective, we encourage CMS to require Medicare Part B and Medicare Part D plans to reduce or eliminate utilization management tools, including step therapy and/or prior authorization barriers to ensure patients are able to quickly access a negotiated drug.

Orphan Drug Exclusion

We acknowledge that the IRA includes a limited exclusion for orphan drugs that only treat one rare disease from drug price negotiation. However, we are concerned CMS' current interpretation of this rare disease exclusion, which makes products eligible for negotiation if they have been designated for two or more orphan diseases – even if the drug is not actually FDA approved to treat the second orphan disease - will disincentivize drug companies from conducting even the basic research necessary to develop a drug for additional rare diseases. Designating a drug for a rare disease is done very early on in the drug development process and does not allow the company to market the drug because it has not been proven to be safe and effective to treat that specific disease. We urge CMS to clarify that obtaining additional designations for a small molecule or biologic will not make a drug negotiation eligible until the drug has been approved by FDA to treat a second disease or condition.

From the rare disease patient community's perspective, successful IRA implementation hinges on a careful balance between greater affordability and maintaining appropriate incentives for continued investment in rare disease specific drug development. We thank CMS for the opportunity to comment on this latest IRA guidance and look forward to working with CMS to ensure rare disease patients and patient advocacy organizations can fully participate within this important effort and benefit from the law.

For questions related to this comment letter, please contact Heidi Ross, Vice President of Policy and Regulatory Affairs at the National Organization for Rare Disorders at HRoss@rarediseases.org.

Thank you for your consideration,

National Organization for Rare Disorders
A Cure in Sight
Alpha-1 Foundation
ALS Association
American Behcet's Disease Association
(ABDA)
American Partnership for Eosinophilic
Disorders

Angelman Syndrome Foundation
Autoimmune Encephalitis Alliance, Inc.
Avery's Hope
Bladder Cancer Advocacy Network (BCAN)
CancerCare
Children's PKU Network
Chondrosarcoma CS Foundation
Choroideremia Research Foundation

Chronic Disease Coalition
Coalition to Cure Calpain 3
Congenital Hyperinsulinism International
Consortium of MS Centers
Cure CMD
Cure HHT
Cure SMA
Cutaneous Lymphoma Foundation
Cystic Fibrosis Research Institute
DADA2 Foundation
Desmoid Tumor Research Foundation
Diann Shaddox Foundation for Essential Tremor
Epilepsy Foundation
FACES: The National Craniofacial Association
FD/MAS Alliance
Fibromuscular Dysplasia Society of America
FOD (Fatty Oxidation Disorders) Family Support Group
Foundation for Sarcoidosis Research
Friedreich's Ataxia Research Alliance (FARA)
Global Liver Institute
Gaucher Community Alliance
Global Healthy Living Foundation
Glut1 Deficiency Foundation
GRIN2B Foundation
Hepatitis B Foundation
Hydrocephalus Association
Hypertrophic Olivary Degeneration Association
IgA Nephropathy Foundation
International Autoimmune Encephalitis Society
International Foundation for Autoimmune & Autoinflammatory Arthritis
International Pemphigus Pemphigoid Foundation
International Waldenstrom's
Macroglobulinemia Foundation
KBG Foundation
Leukodystrophy Newborn Screening Action Network
LGMD Awareness Foundation, Inc
Li-Fraumeni Syndrome Association (LFS Association / LFSA)

LUNgevity Foundation
Lymphangiomatosis & Gorham's Disease Alliance
MdDS Balance Disorder Foundation
MLD Foundation
Muscular Dystrophy Association
Myasthenia Gravis Foundation of America
Myocarditis Foundation
National Ataxia Foundation
National Bone Marrow Transplant Link
National MALS Foundation
National Oncology State Network
National PKU News
National Scleroderma Foundation
NBIA Disorders Association
NR2F1 Foundation
NTM Info & Research
Organic Acidemia Association
Phaware Global Association
Phelan-McDermid Syndrome Foundation
Project Alive
PWSA | USA
Reflex Sympathetic Dystrophy Syndrome Association
RETpositive
SATB2 Gene Foundation
Spastic Paraplegia Foundation
SSADH Association
Super T's Mast Cell Foundation
Superficial Siderosis Research Alliance
Syngap 1 Foundation
TargetCancer Foundation
Tatton Brown Rahman Syndrome Community
TEAM TELOMERE
Texas Prader Willi Association
The Akari Foundation
The Avalon Foundation
The Global Foundation for Peroxisomal Disorders
The Jansen's Foundation
The Life Raft Group
The Mast Cell Disease Society
The Multiple System Atrophy Coalition
The RYR-1 Foundation
Thrive with Pyruvate Kinase Deficiency Organization

United MSD Foundation
United Porphyrins Association
Usher 1F Collaborative
Usher Syndrome Coalition
Usher Syndrome Society

Vasculitis Foundation
Vestibular Disorders Associations
wAIHA Warriors
Xia -Gibbs Society



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April 14, 2023

The Honorable Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244

Submitted Electronically via: IRAREbateandNegotiation@cms.hhs.gov

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Deputy Administrator Seshamani:

The National Pharmaceutical Council (NPC) appreciates the opportunity to submit comments regarding the Centers for Medicare & Medicaid Services (CMS) Guidance, *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments* (Guidance or the Guidance).

NPC is a health policy research organization dedicated to the advancement of good evidence and science and to fostering an environment in the United States that supports medical innovation. We have rich experience conducting research and disseminating information about the critical issues of evidence, innovation and the value of medicines for patients. Our research helps inform important healthcare policy debates and supports the achievement of the best patient outcomes in the most efficient way possible.

NPC's research and that of others have found that public policies that reduce the incentives to invest in research and development result in less innovation, fewer treatment options, and lower life expectancy.¹ The Inflation Reduction Act (IRA or the Act) creates a new price-setting

¹ Ciarametaro M and Buelt L. Assessing the effects of biopharmaceutical price regulation on innovation. 2022. <https://www.npcnow.org/resources/assessing-effects-biopharmaceutical-price-regulation-innovation>; Thomas A. Abbott & John A. Vernon, 2007. "The cost of US pharmaceutical price regulation: a financial simulation model of R&D decisions," Managerial and Decision Economics, John Wiley & Sons, Ltd., vol. 28(4-5), pages 293-306.; Leonard D. Schaeffer Center for

mechanism that will change the economic incentives for bringing new medicines to market, and evidence suggests manufacturers are already responding to those incentives.²

An important goal in implementation of the Act should be to set guidance that, to every extent possible, minimizes the deleterious impact of the IRA on the incentives for the development of innovative therapies as well as patient access. Unfortunately, we believe the Guidance does the opposite.

The price-setting mechanism described in the Guidance, incorrectly portrayed as “negotiation,” lacks clear standards for the evidence that will be used in the process and the transparency necessary for the public to reproduce or evaluate CMS’s process and decisions. It also minimizes the opportunity for patients, providers and other clinical experts to inform and participate continuously in the process. Furthermore, the effectuation of the Maximum Fair Price (MFP) and Part D formulary inclusion of selected drugs are built on a chassis ripe with perverse incentives and opportunities for fraud and abuse and provide minimal opportunity to prevent and detect unsavory activities.

The importance of implementing the price-setting provisions of the IRA in a manner that accurately values medicines and maintains patient access cannot be overstated. This new process forces manufacturers to accept CMS’s final price, face an unreasonable excise tax, or exit the market – all of which threaten the development of, and patient access to, new treatments or cures.

We understand that CMS has a statutory requirement to implement the IRA. We also note that many NPC members have long argued that the underlying structure of the negotiation program, as set forth by the statute and implemented here by CMS, is legally flawed. In review of the punishing penalties for non-compliance, and the general inflexibility of the process for product selection and maximum fair price (MFP) implementation, these legal flaws cannot be overcome through general guidance clarity at this stage.

Nevertheless, NPC appreciates the opportunity to provide input and provides herein several suggestions for CMS to consider that might be helpful in the transparency objective of the Agency as it implements this program. None of these resolve the more fundamental legal infirmities of the overall program, nor could they. NPC’s recommendations are summarized on the following pages:

Health Policy & Economics. Annual Report 2020. <https://healthpolicy.usc.edu/wp-content/uploads/2021/03/Schaeffer-Center-2020-Annual-Report.pdf>

² Grogan J. (2022) The Inflation Reduction Act Is Already Killing Potential Cures. WSJ. <https://www.wsj.com/articles/the-inflation-reduction-act-killing-potential-cures-pharmaceutical-companies-treatment-patients-drugs-prescriptions-ira-manufacturers-11667508291> Longo, N. (2023). WTAS: Inflation Reduction Act already impacting R&D decisions. PhRMA. Available at: <https://catalyst.phrma.org/wtas-inflation-reduction-act-already-impacting-rd-decisions>; Powaleny, Andrew. (2023). IRA Impacts: Cancer treatment research and development. PhRMA. Available at: <https://catalyst.phrma.org/ira-impacts-cancer-treatment-research-and-development>; Longo, N. (2023). WTAS: Inflation Reduction Act already impacting R&D decisions. PhRMA. Available at: <https://catalyst.phrma.org/wtas-inflation-reduction-act-already-impacting-rd-decisions>; IRA survey: Biotechs bracing for impact. Biocentury. March 16, 2023.

I. (Section 40) Requirements for Manufacturers of Selected Drugs

- Allow the public to review the comments provided in response to the Guidance, as soon as possible after the end of the comment period while protecting the confidentiality and security of proprietary information.
- Remove the restrictions on manufacturers disclosing written or verbal information from CMS's offers or counteroffers, and the requirement that manufacturers destroy this information after the process is complete. This requirement deprives the public from learning about CMS's process and priorities and disadvantages manufacturers who may someday need to renegotiate with CMS.
- Provide manufacturers with Prescription Drug Event (PDE) data to verify the MFP is being provided only to MFP-eligible individuals.
- Commit to ensuring that providers report a "minimally necessary"³ data set to the manufacturer or its vendor to be entitled to access the MFP.
- Abandon the burdensome and unworkable Primary/Secondary Manufacturer policy.

II. (Sections 50 and 60) Negotiation Factors and Process

- Implement these sections with maximum transparency to provide manufacturers and other stakeholders the opportunity to inform, evaluate, and predict CMS's process and priorities in the overall negotiation process and the individual negotiations for selected drugs.
- Provide clarity on the choices of therapeutic alternative for each approved indication of selected drugs and ground those choices in current, evidence-based clinical practice. CMS should focus on clinical benefits and cost offsets when comparing treatments and determining value, and not reduce the preliminary price by information unrelated to the value of a treatment (e.g., cost-recovery, remaining exclusivity, etc.).
- Develop, communicate, and implement clear definitions of unmet need consistent with relevant patient populations' needs for each indication of selected drugs.
- Engage with patients and caregivers throughout the process to gain insights into the value, preferences for appropriate treatment, and the indirect costs that patients and their families bear, to inform the evaluation of the clinical benefit of a selected drug (evaluation process). It is essential to gain patient input to identify unmet needs, therapeutic alternatives, clinical and humanistic benefits.
- Create and implement a consistent framework that provides more information about how CMS will make decisions during the negotiation process, including the identification of therapeutic alternatives, a broader definition of unmet medical need, stakeholder involvement, and the evidence used to support CMS decisions. This information should be well-known before CMS begins its process, and the relative importance of these factors should be published in the final determination of the MFP.
- Apply well-established best practices for evidence evaluations from organizations including the Innovation and Value Initiative and ISPOR, the Professional Society for Health Economics and Outcomes Research. Provide clarity into the evidence standards

³ <https://www.hhs.gov/hipaa/for-professionals/faq/455/does-hipaa-permit-health-plans-to-disclose-information-to-pharmaceutical-manufacturers/index.html>

that CMS will use at all steps of the process, including when working with external organizations.

- CMS is making significant changes to Medicare policy and seeking to implement a complicated process in a short amount of time. In the interest of not harming patients' access to medicine – and the innovation ecosystem that creates new medicine - we encourage CMS to take the time needed to build a transparent and consistent process and methodology and to set prices at the ceiling price for initial price applicability year (IPAY) 2026.

III. **(Section 110) Part D Formulary Inclusion of Selected Drugs**

- At a minimum, CMS should ensure people with Medicare do not experience decreased formulary access as a result of implementation.

We elaborate on these recommendations below.

(Section 40) Requirements for Manufacturers of Selected Drugs

A. Improving Transparency in the Implementation Process

The implementation of the Inflation Reduction Act (IRA) is the most significant prescription drug pricing intervention in the history of the Medicare program. It is being closely followed by those who invest in, research, and develop new cures. It is also being closely watched by health policy experts, pharmacoeconomic researchers, patient advocates, and others. CMS has a long history of publishing and responding to information provided by stakeholders when implementing new policies. Though the IRA text permitted implementation of the price-setting process via guidance, this Guidance opens CMS to criticism for creating an opaque process giving the agency maximum flexibility and latitude while failing to provide adequate clarity and details about how it will implement important provisions (e.g., identification of therapeutic alternatives, weighting of factors for initial offer, etc.).

We appreciate CMS communicating separately from the Guidance that it will make comments in response to the Guidance publicly available. CMS should allow the public to review the comments provided in response to the Guidance as soon as possible after the comment period ends, while protecting the confidentiality and security of proprietary information. Furthermore, CMS should respond to suggestions and comments provided in response to the Guidance to allow experts to evaluate the decisions made by CMS and the information on which these decisions were made. Depriving researchers and the public of the opportunity to learn from and provide continued input to this process is contrary to CMS's historical transparency and stakeholder engagement.

CMS should abandon the proposed data use provisions to enhance transparency, increase public confidence, and facilitate collaboration with manufacturers. Specifically, CMS should abandon the "data use provisions and limitations" that would prohibit manufacturers from disclosing information exchanged verbally or in writing about the agency's MFP decision-

making process. Scientific sessions attended by pharmacoeconomic researchers, managed care pharmacists, actuaries, and others are already rich with IRA content, and audiences are asking important questions about how the law will be implemented. Understanding what information CMS reviews, values, or excludes in the context of individual negotiations as well as with regard to the general process is essential to the advancement of learning in these disciplines.

More clarity about and transparency into this process also encourages industry scientists to create good pharmacoeconomic evidence during the drug development process. As useful pharmacoeconomic evidence takes time and money to create, it is important for all manufacturers to know what information CMS did or did not value during previous negotiations. Restricting the use of this information also prevents manufacturers from referring to these discussions when participating in the renegotiation process described in the statute but not included in this guidance.

Simply stated, squelching conversation between these disciplines not only hurts science; it also undermines the credibility of the agency's decision-making and further exposes it to public criticism.

B. Decreasing the Potential for Payment Errors, Fraud, and Perverse Incentives

We commend CMS for its desire to provide patients with access to the MFP at point of sale and for providing flexibility for manufacturers with MFP agreements to provide access to the MFP. As CMS heard in comments provided in response to the Office of the Inspector General's regulations to remove the safe harbor protection for prescription drug rebates, it is important to contemplate the workability of these new mechanisms.

NPC has a deep understanding of the pharmaceutical supply chain. As such, we have concerns and suggestions about the flow of funds and lack of data described in Section 40.4 (and the corresponding paragraphs in Section 90.2). Simply stated, the Guidance robustly describes manufacturer noncompliance, yet only offers one sentence about dispenser noncompliance. CMS should clarify that manufacturers require access to data or other mechanisms to verify eligibility or otherwise evaluate the process for providing access to MFP. Manufacturers should not be the only stakeholders (e.g., pharmacies, mail order services, and other dispensers) in the supply chain identified if an MFP is not made available to beneficiaries. CMS should monitor compliance across all parties if they proceed with establishing a toll-free phone line and email box that accepts claims of MFP non-compliance.

The pharmacy's actual acquisition cost is not known to or controlled by manufacturers, and the existing chargeback payments and rebate mechanisms are currently inadequate to effectuate the MFP, given the statutory responsibilities to provide access to the MFP and the 340B nonduplication provision. If, in the example CMS provides, the pharmacy's purchase price increased (or was reported to be higher) and the MFP remained constant, the amount of the reimbursement required from the manufacturer would increase. Likewise, if a prescription was

filled, billed, and returned to stock within the 14-day time frame proposed by CMS, the Part D plan would have the information necessary to reverse their payment to the pharmacy, but the manufacturer would not be aware of the need to reverse the MFP effectuation payment. This creates a significant economic incentive that could encourage inadvertent duplicate discounts or outright diversion or fraud that threatens the integrity of IRA implementation.

As such, we believe the 14-day timeframe proposed is unreasonable for manufacturers, and CMS should provide manufacturers with access to Prescription Drug Event (PDE) data to verify eligibility and base the MFP discount on a consistent, more widely available metric like Wholesale Acquisition Cost. CMS could also consider designating a third-party administrator to oversee this process for manufacturers choosing a retrospective approach.

Likewise, a lack of transparency in the 340B Drug Pricing Program, the potential for mixing mechanisms of chargebacks and rebates of 340B and MFP on the same National Drug Code (NDC), and the inconsistent timeframe and methods by which pharmacy claims are determined as 340B eligible, creates a significant potential for MFP and 340B duplicate discounts. Without additional verification from CMS, manufacturers will need to validate that 340B entities are only providing the MFP to eligible individuals.

To avoid duplication of 340B and MFP prices, CMS should require identification of 340B units at the point of sale at the time of dispensing (when the claim is created). The Agency should also commit to ensuring that providers report a “minimally necessary” data set to the manufacturer or its vendor to be entitled to access the MFP and for the purposes of validating their right to access in a timely manner, according to standard business practices and consistent with non-duplication requirements. CMS should expressly acknowledge that manufacturers will establish, receive, review, and, as necessary, audit MFP validation data to ensure MFP access is provided in accordance with the statute.

Given the complex interactions of the processes described above, CMS could establish a clearinghouse-type organization to identify 340B units dispensed or administered to Medicare enrollees. The 340B clearinghouse would act as a claims verifier, reviewing Part D PDE data as well as data submitted by 340B covered entities (or entities acting on their behalf) to confirm whether a claim is subject to a 340B agreement, similar to the role played by 340B third-party administrators (TPAs) and split-billing vendors today.

C. Primary/Secondary Manufacturer Definition

NPC suggests that CMS abandon the Primary/Secondary Manufacturer policy. The primary and secondary manufacturer concept developed by CMS is unworkable, impractical, and not supported by the statute. Requiring one manufacturer to enter into an agreement with CMS that holds them responsible for the actions of another manufacturer (and potentially a competitor) unnecessarily complicates implementation and exposes manufacturers to potentially significant burden.

I. (Sections 50 and 60) Negotiation Factors and Process

As stated earlier, many stakeholders are closely watching CMS's IRA implementation process. The price-setting process adopted for the first IPAY will be closely studied not just by manufacturers, but by the broader pharmacoeconomic, health policy, and patient advocacy communities. The credibility of CMS's process will be judged by the agency's use of good evidence and appropriate methods in a transparent and patient-centered process.

CMS has described a domestic reference price-setting mechanism that begins by identifying a therapeutic alternative and using its price as an initial starting point before adjusting for clinical benefits to achieve a preliminary price that is further adjusted by a variety of other factors unrelated to the value of a treatment.

We do not believe the Guidance describes a satisfactory process to determine the value of a medicine or set its price and note that it resembles processes used by countries outside of the United States that face significant delays in accessing innovation. We believe that only clinical benefit, health improvement and cost offsets associated with the treatment may be used to determine the value of a medicine. Adjusting reimbursement by the elements described in the manufacturer data elements (e.g., R&D costs, cost of production, patent life or exclusivity) will have disastrous effects on innovation and deny patients future treatments or future indications for existing treatments.

The statute requires CMS to use a "consistent methodology and process" for negotiation.⁴ More clarity is needed than is provided in the Guidance to achieve that goal, especially related to the identification of therapeutic benefit and the weighting of factors used to determine the preliminary price and initial offer. Only when such clarity is provided can manufacturers and external stakeholders build their own models to anticipate, inform, and evaluate the process CMS operationalizes. Manufacturers in particular need more clarity to accurately prepare their submissions and meaningfully participate in the process.

As previously stated, CMS is making significant changes to Medicare policy and seeking to implement a complicated process in a short amount of time. In the interest of not harming patients' access to medicine – and the innovation ecosystem that creates new medicine – we encourage CMS to take the time needed to build a transparent and consistent process and methodology and to set prices at the ceiling price for IPAY 2026. Specific recommendations follow.

A. Development of a Transparent and Rigorous Evaluation and Price-Setting Process

NPC encourages CMS to implement a transparent and inclusive evaluation process to promote credibility and support for their price-setting and counteroffer process. The agency is introducing comparative effectiveness to the Medicare program and making value determinations when establishing a "preliminary price" for selected drugs. A large and growing

⁴ SSA § 1194(b)(1).

body of research and guidance emphasizes the critical nature of transparency and methodological rigor during value assessment.⁵ CMS should pursue analytic transparency by carefully considering data assumptions and highlighting the limitations and uncertainties of analyses to the public. By providing robust information about its evaluation criteria and the factors considered during the price-setting process, CMS can help build trust with all stakeholders and allow others to evaluate their process. Specifically, NPC encourages:

- **Engagement with key stakeholders throughout the assessment process** to ensure all perspectives are considered and have the opportunity to inform the assessment.⁶ CMS should specifically seek and incorporate stakeholder feedback about their choice of therapeutic alternatives for each selected drug; the benefits of a selected drug to each stakeholder (including patients, clinicians, caregivers, manufacturers and other scientists); the meaning of unmet need to each stakeholder and the extent to which a selected drug meets that unmet need.⁷

CMS should seek patient input via a variety of mechanisms as the Information Collection Request process may not be the best way to reach this important stakeholder community. Given the important perspectives of patients and caregivers, we provide additional recommendations on meaningful patient input to the CMS process determining clinical benefit throughout this comment. Furthermore, manufacturers should be able to inform the selection of evidence about their products and verify information provided about their products from others.

- **The use of public comment periods during the negotiation process** with sufficient time to review materials and submit comments as well as transparency around how comments are considered and used or not used by the agency. The public has been given the ability to provide comments and read agency responses on policies with far

⁵ Berger ML, Sox H, Willke RJ, Brixner DL, Eichler HG, Goettsch W, Madigan D, Makady A, Schneeweiss S, Tarricone R, Wang SV, Watkins J, Mullins CD. Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making. *Value Health*. 2017 Sep;20(8):1003-1008.; National Pharmaceutical Council. Guiding Practices for Patient-Centered Value Assessment. 2021. Washington, DC. Available at: <https://www.npcnow.org/sites/default/files/2021-04/npc-guiding-practices-for-patient-centered-value-assessment.pdf>; Drummond M, Schwartz JS, Jansson B, Luce BR, Neumann BR, Seibert U, Sullivan SD. Principle 10. Key Principles for the Improved Conduct of Health Technology Assessments for Resource Allocation Decisions. *International Journal of Technology Assessment in Health Care*. 2008. 24:3:250.; Oortwijn W, Husereau D, Abelson J, Barasa E, Bayani DD, Canuto Santos V, Culyer A, Facey K, Grainger D, Kieslich K, Ollendorf D, Pichon-Riviere A, Sandman L, Strammiello V, Teerawattananon Y. Designing and Implementing Deliberative Processes for Health Technology Assessment: A Good Practices Report of a Joint HTAi/ISPOR Task Force. *Value Health*. 2022 Jun;25(6):869-886.; OMB, Circular A-4, Regulatory Analysis (April 6, 2023). Available at: <https://www.whitehouse.gov/wp-content/uploads/2023/04/DraftCircularA-4.pdf> (Circular A-4).

⁶ Drummond M, Schwartz JS, Jansson B, Luce BR, Neumann BR, Seibert U, Sullivan SD. Key Principles for the Improved Conduct of Health Technology Assessments for Resource Allocation Decisions. *International Journal of Technology Assessment in Health Care*. 2008. 24:3:250.; Luce BR, Drummond MF, Dubois RW, Neumann PJ, Jönsson B, Siebert U, Schwartz JS. Principles for planning and conducting comparative effectiveness research. *J Comp Eff Res*. 2012 Sep;1(5):431-40; Oortwijn W, Husereau D, Abelson J, et al. Designing and Implementing Deliberative Processes for Health Technology Assessment: A Good Practices Report of a Joint HTAi/ISPOR Task Force. *Int J Technol Assess Health Care*. 2022;38(1).

⁷ Khavjou O, Bradley C, D'Angelo S, Buell N, Giombi K, Honeycutt A. Landscape Review and Summary of Patient and Stakeholder Perspectives on Value in Health and Health Care. August 2022. Available at: <https://www.pcori.org/sites/default/files/PCORI-Landscape-Review-Summary-Patient-Stakeholder-Perspectives-Value-Health-Health-Care-August-2022.pdf>

less patient impact, presumably not solely because of the Administrative Procedures Act but because it is the right thing to do. Public comments should be sought and published in an annual docket containing all key documents and decision points in an evaluation such as scoping documents, analytic protocols, and draft reports. Allowing sufficient time for interested stakeholders, including manufacturers of selected drugs, to review materials and prepare comments ensures that stakeholders can thoughtfully and comprehensively respond to the comment request. Providing transparency around how comments are addressed builds credibility and trust in the process.

- **Transparent and reproducible methods and results** to the extent possible, given the confidentiality required for proprietary information, methods, models (including all calculations). Assumptions should be transparent to interested stakeholders. This transparency, combined with the ability to reproduce results, will further build credibility and trust in the process.⁸ Importantly, before negotiation begins, CMS should create and publish its decision-making framework – both generally and for selected drugs – which should include, at a minimum, information on:
 1. the therapeutic alternative(s) considered for each indication for selected drugs and the rationale for selection;
 2. the definition(s) of unmet need for each indication of selected drugs;
 3. the full range of benefits and impacts considered for each indication;
 4. the internal process and rationale for determining which benefits and impacts were included;
 5. a list of each stakeholder consulted;
 6. the source(s) of evidence considered, particularly clinicians and patients;
 7. how each benefit and impact considered influenced the final MFP, to include any algorithms, calculations, or modeling that related to MFP determination, as well as rationale for evidence that was not considered; and
 8. the limitations of the data collected and uncertainties in CMS’s decision-making. As is common in any rigorous, evidence-based process, this information should also be made clear when reported to the public.

These elements of CMS’s evaluation and MFP determination should be made public at distinct phases of evaluation. First, this draft framework should be made public as a scoping document prior to initiating stakeholder engagement and beginning data collection for CMS’s evaluation process. Secondly, preliminary results should be shared with manufacturers of selected drugs at least 60 days prior to initiating the negotiation process. Finally, results of this framework should be revealed to the public to explain the final MFP. Importantly, CMS should publish the required IPAY 2026 MFP explanations before IPAY 2027 negotiations begin.

⁸ Drummond M, Schwartz JS, Jansson B, Luce BR, Neumann BR, Seibert U, Sullivan SD. Key Principles for the Improved Conduct of Health Technology Assessments for Resource Allocation Decisions. *International Journal of Technology Assessment in Health Care*. 2008. 24:3:250.; Neumann PJ, et al. A Call for Open-Source Cost-Effectiveness Analysis. *Ann Intern Med*. 2017 Sep 19;167(6):432-433; Luce BR, Drummond MF, Dubois RW, Neumann PJ, Jönsson B, Siebert U, Schwartz JS. Principles for planning and conducting comparative effectiveness research. *J Comp Eff Res*. 2012 Sep;1(5):431-40.

- **Robust engagement with manufacturers** consistent with the practices and policies of other payers and regulators.⁹ Given their vast knowledge of their products and therapeutic areas, pharmaceutical manufacturers and their pharmacoeconomic researchers are critically important sources of information on the value of treatments for payer decision-making. Recognizing this, Congress and the U.S. Food and Drug Administration (FDA) have provided guidelines on how healthcare economic information (HCEI) can be provided to payers' pharmacy and therapeutics committees.¹⁰ We encourage CMS to similarly provide opportunities for meaningful engagement with manufacturers. Existing industry best practices suggest the *minimum level* of engagement with manufacturers of selected drugs would be to meet with agency staff at three specific points during the MFP process: 1) after drug selection but prior to initiation of the price-setting process; 2) prior to CMS presenting the initial offer; and 3) the three meetings described by CMS as occurring after CMS presents the initial offer. All meetings should be offered as in-person, and we refer back to our comments on Section 40 about the importance of lessons learned during this process.

1. Evaluation of data on product value for quality, particularly information on patient experience

The Guidance states that CMS will accept information on the benefits of selected drugs from the public and conduct its own literature reviews and database analyses. Open public submission of evidence is laudable and helpful, as stakeholders may have pertinent evidence that is not available in the published literature, or evidence which was not properly identified in the initial literature review. However, public submission comes with a cost of sorting through and identifying studies that are both high quality and relevant to the therapeutic alternatives and patient population.¹¹

The results of an assessment depend on the evidence that underlies it, and the burden is on CMS to use and develop evidence in a systematic, transparent, and robust manner. To maximize credibility and trust in the assessment process, the procedures by which evidence is identified and included in the assessment should be objective, systematic, transparent, robust, reproducible, and made public as part of the scoping process. Not following widely accepted scientific best practices erodes trust in the process.

⁹ Smith JC, Snider DE, Pickering LK; Advisory Committee on Immunization Practices. Immunization policy development in the United States: the role of the Advisory Committee on Immunization Practices. *Ann Intern Med.* 2009 Jan 6;150(1):45-9.; Payer Engagement in HEOR. Ispor.org. Available at: <https://www.ispor.org/strategic-initiatives/payer-engagement-in-heor>

¹⁰ Section 3630, "Facilitating Exchange of Product Information Prior to Approval" of H.R. 2617, Consolidated Appropriations Act, 2023; FDA. Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities Questions and Answers Guidance for Industry and Review Staff.; 2018. Available at: <https://www.fda.gov/media/133620/download>.

¹¹ Drummond M, Schwartz JS, Jansson B, Luce BR, Neumann BR, Seibert U, Sullivan SD. Principle 10. Key Principles for the Improved Conduct of Health Technology Assessments for Resource Allocation Decisions. *International Journal of Technology Assessment in Health Care.* 2008. 24:3:250.; Luce BR, Drummond MF, Dubois RW, Neumann PJ, Jönsson B, Siebert U, Schwartz JS. Principles for planning and conducting comparative effectiveness research. *J Comp Eff Res.* 2012 Sep;1(5):431-40.

Accordingly, we encourage CMS to develop robust, transparent standards for both submitted and internally generated data to ensure that evidence is methodologically rigorous and apply these same rigor and transparency standards to the agency's internal claims analysis and review when adjusting the MFP initial starting point based on clinical evidence. These standards can be informed by using accepted rubrics for evaluating study quality.¹² Evidence can be of varying quality and certainty, and the findings from individual studies can conflict with each other. To produce a meaningful and credible assessment, accepted methods should be used to evaluate quality and certainty of evidence and to determine how to handle conflicting evidence.¹³ Grading rubrics should be fit for purpose and most appropriate for the type of evidence (e.g., clinical versus economic data). Procedures for evaluating evidence quality should be included in scoping documents, and the results should be made available through the value assessment.

We encourage CMS to follow and tailor as necessary consensus guidance on the conduct and evaluation of comparative effectiveness research (CER) that is both submitted and internally conducted.¹⁴ Principles of good CER adopt elements of high-quality research methods, including: clear statements of objectives; transparency of process, data and methods; engagement of stakeholders and analytic perspectives reflecting multiple stakeholders; use of comparators relevant to current clinical practice; evaluation of outcomes relevant to the stated objectives; and explicit treatment of heterogeneity and uncertainty.

2. Inclusion of Treatment Costs and Cost Offsets

Costs should be representative of the net price most relevant to the user. Cost offsets are a driving component of drug value and actual transaction costs, and care should be taken to ensure that costs are as representative of the actual net cost to the payer and net revenue realized by the manufacturer as possible in order to achieve an accurate assessment. For biopharmaceuticals, following ISPOR good research practices for measuring drug costs can help

¹² Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. *Value Health*. 2022 Jun;25(6):1060.; von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007 Oct 20;370(9596):1453-7.; The GRACE Checklist: A Validated Assessment Tool for High Quality Observational Studies of Comparative Effectiveness. *J Manag Care Spec Pharm*. 2016 Oct;22(10):1107-13.; Luce BR, Drummond MF, Dubois RW, Neumann PJ, Jönsson B, Siebert U, Schwartz JS. Principles for planning and conducting comparative effectiveness research. *J Comp Eff Res*. 2012 Sep;1(5):431-40.

¹³ Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. *Value Health*. 2022 Jun;25(6):1060.; von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007 Oct 20;370(9596):1453-7.

¹⁴ Berger ML, Sox H, Willke RJ, Brixner DL, Eichler HG, Goettsch W, Madigan D, Makady A, Schneeweiss S, Tarricone R, Wang SV, Watkins J, Mullins CD. Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making. *Value Health*. 2017 Sep;20(8):1003-1008.; Dreyer NA, Bryant A, Velentgas P. The GRACE Checklist: A Validated Assessment Tool for High Quality Observational Studies of Comparative Effectiveness. *J Manag Care Spec Pharm*. 2016 Oct;22(10):1107-13.; Luce BR, Drummond MF, Dubois RW, Neumann PJ, Jönsson B, Siebert U, Schwartz JS. Principles for planning and conducting comparative effectiveness research. *J Comp Eff Res*. 2012 Sep;1(5):431-40.

achieve this objective.¹⁵ In the case of MFP, CMS must ensure that cost data reflects discounts and rebates provided to Medicare and recognize that the net cost to the payer does not always represent the net revenue realized by the manufacturer.

We encourage CMS to also include comprehensive assessments of the economic benefits of selected drugs, in addition to the costs of the treatments themselves. In any assessment of the value of medical treatments, all healthcare costs and cost offsets should be included.¹⁶ Treatments may have up-front costs that lead to long-term improvements in patient health. Those improvements may yield “cost offsets,” or savings due to reductions in resource needs, such as reduced hospitalizations. The full value of treatment can only be assessed by including both the treatment costs and cost offsets it may produce. Only considering the treatment costs but not the potential cost offsets would lead to an incomplete assessment of value.

When evaluating cost data, the time horizon should be long enough to incorporate the benefits of the treatment and the lower costs of medications when they become generic. Many of the cost-offset benefits of treatment, such as costs of avoided hospitalizations, show up in the longer-term. To measure the full value of a treatment, the time horizon for costs should be long enough to capture these cost offsets,¹⁷ and to account for the lower costs of medications when generics and biosimilars are introduced.

3. Utilization of Best Practices Relevant to CMS’s Proposed Evidence Evaluation

We have cited in this response several publications on research best practices relevant to the agency’s evidence evaluation proposed in the Guidance. We encourage CMS to review and, wherever possible, utilize the guiding principles listed below to ensure the transparency, validity, and credibility of the annual price-setting process. In our foregoing recommendations, we have emphasized methodological issues that are relevant to the price-setting process proposed by CMS. We encourage CMS to consider these tools to the extent that the principles are appropriate for Medicare:

- *NPC’s Guiding Practices for Patient-Centered Value Assessment* includes 28 specific elements surrounding six key aspects of value assessment, including the assessment process, methodology, benefits, costs, evidence, and dissemination and utilization.¹⁸
- *Principles for planning and conducting comparative effectiveness research*, published by NPC researchers alongside a team of international collaborators, highlights thirteen principles for planning and conducting comparative effectiveness research.¹⁹

¹⁵ Hay JW, Smeeding J, Carroll NV, et al. Good research practices for measuring drug costs in cost effectiveness analyses: issues and recommendations: the ISPOR drug cost task force report – Part I. *Value Health* 2010;13:3-7.

¹⁶ Drummond M, Schwartz JS, Jansson B, Luce BR, Neumann BR, Siebert U, Sullivan SD. Key Principles for the Improved Conduct of Health Technology Assessments for Resource Allocation Decisions. *International Journal of Technology Assessment in Health Care*. 2008. 24:3:250.

¹⁷ Hay JW, Smeeding J, Carroll NV, et al. Good research practices for measuring drug costs in cost effectiveness analyses: issues and recommendations: the ISPOR drug cost task force report – Part I. *Value Health* 2010;13:3-7.

¹⁸ National Pharmaceutical Council. *Guiding Practices for Patient-Centered Value Assessment*. 2021. Washington, DC. Available at: <https://www.npcnow.org/sites/default/files/2021-04/npc-guiding-practices-for-patient-centered-value-assessment.pdf>

¹⁹ Luce BR, Drummond MF, Dubois RW, Neumann PJ, Jönsson B, Siebert U, Schwartz JS. Principles for planning and conducting comparative effectiveness research. *J Comp Eff Res*. 2012 Sep;1(5):431-40.

- *The Myth of Average: Why Individual Patient Differences Matter*, published by NPC, provides recommendations for ways improving the patient-centeredness of value assessment.²⁰
- ISPOR and the International Society for Pharmacoeconomics and Epidemiology (ISPE) have published good practices for real-world data studies of comparative effectiveness with the goal of providing a trustworthy foundation for use of RWE in decision-making.²¹
- *Key principles for the improved conduct of health technology assessments for resource allocation decisions*, published by a leading team of value assessment experts, offers a set of 15 principles for health technology assessments.²²
- The Innovation and Value Initiative provides recommendations applying the tools of value assessment, with an emphasis on consensus among stakeholder communities.²³
- PhRMA's *Principles for Value Assessment Frameworks* offers 15 principles tailored to meeting patient needs and improving healthcare decision-making.²⁴
- *Domains of Patient Centeredness in Value Assessment*, authored by the National Health Council (NHC), highlights the key areas for healthcare stakeholders to focus on when implementing patient perspectives in value assessments.²⁵
- The NHC also created a Patient-Centered Value Model Rubric for healthcare stakeholders to assess the use of patient centeredness in value model development and to guide model developers on how to implement patient engagement throughout the value modeling process.²⁶

B. Identification of Therapeutic Alternatives

The IRA instructs CMS to consider “the extent to which [a selected drug] represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives”; however, it does not suggest that the cost of those alternatives should be used as a benchmark for an initial offer. The Guidance diverges from the statute because CMS intends to rely on Part D net price(s) or the Part B ASP of therapeutic alternatives “to determine a starting point for developing an initial offer.”²⁷

²⁰ National Pharmaceutical Council. *The Myth of Average: Why Individual Patient Differences Matter*. 2022. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2022-01/The_Myth_of_Average_01.2022.pdf

²¹ Berger ML, Sox H, Willke RJ, Brixner DL, Eichler HG, Goettsch W, Madigan D, Makady A, Schneeweiss S, Tarricone R, Wang SV, Watkins J, Mullins CD. Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making. *Value Health*. 2017 Sep;20(8):1003-1008.

²² Drummond M, Schwartz JS, Jansson B, Luce BR, Neumann BR, Seibert U, Sullivan SD. Principle 10. Key Principles for the Improved Conduct of Health Technology Assessments for Resource Allocation Decisions. *International Journal of Technology Assessment in Health Care*. 2008. 24:3:250.

²³ Innovation and Value Initiative. Principles for Value assessment in the US. <https://thevalueinitiative.org/principles-for-value-assessment-in-the-us/>

²⁴ PhRMA. (2016). Principles for Value Assessment Frameworks. Available at: <https://phrma.org/resource-center/Topics/Cost-and-Value/Principles-for-Value-Assessment-Frameworks>

²⁵ National Health Council. Domains of Patient Centeredness in Value Assessment. 2020. Available at: https://nationalhealthcouncil.org/wp-content/uploads/2020/03/NHC-One-Pagers_Domains.pdf

²⁶ National Health Council. (2016). The Patient Voice in Value: The National Health Council Patient-Centered Value Model Rubric. Available at: <https://nationalhealthcouncil.org/wp-content/uploads/2020/11/20160328-NHC-Value-Model-Rubric-final.pdf>; National Health Council. (2021). Value Classroom. <https://nationalhealthcouncil.org/education/value-classroom/>

²⁷ SSA § 1194(e)(2)(A).

In any assessment of the relative clinical or economic benefits of a drug, the choice of the comparator is a fundamental driver in the outcomes and validity of the assessment with significant implications for patients, payers, and prescribers.²⁸ NPC recommends that the choice of comparators/therapeutic alternatives be driven by clinical appropriateness, informed by current treatment practices among a relevant patient population, and selected from potential comparators with the same treatment modality and class, rather than be dictated by cost, other concerns or implicit goals.²⁹ The selection of a less-costly therapeutic alternative lacking the safety, efficacy, and other clinical benefits of a selected drug – solely to lower the initial starting point of the price-setting process – fails to recognize the value of modern treatments and threatens to reverse the incentives that currently encourage innovation and access.

The use of a comparator that is not consistent with current clinical practice for given patients injects significant biases into the results and recommendations of a comparative assessment. Real world treatment decisions are based on numerous factors associated with the underlying disease and its severity, general health status or frailty, quality of life, and patient preferences.

The Agency for Healthcare Research and Quality's (AHRQ) Effective Health Care Program has produced guidance that may be helpful for CMS.³⁰ Specifically, the book reviews comparator selection in observational CER, noting that comparators “should reflect clinically meaningful choices in real-world practice and be chosen based on the study question being addressed.” AHRQ details how treatment selection bias (i.e., confounding by indication) may arise when disease severity, age, or other underlying health status differ between patients prescribed the drug being evaluated and the drug used as a comparator. The biases introduced by these factors can be minimized by choosing a comparator that has the same indication, similar contraindications, similar adverse effects, and the same treatment modality, class, and mechanism of action.

AHRQ also notes that selection of a comparator of the same treatment modality and class may result in less bias than comparison across modalities or classes.³¹ We appreciate CMS's intent to begin identifying therapeutic alternatives within the same drug class based on chemical class, therapeutic class, or mechanism of action before considering therapeutic alternatives in other classes, and encourage CMS to prioritize reducing bias in treatment comparisons by identifying

²⁸ Berger ML, Sox H, Willke RJ, et al. Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making. *Value in Health*. 2017;20(8):1003-1008.

²⁹ Jaime Caro J, Eddy DM, Kan H, Kaltz C, Patel B, Eldessouki R, Briggs AH; ISPOR-AMCP-NPC Modeling CER Task Forces. Questionnaire to assess relevance and credibility of modeling studies for informing health care decision making: an ISPOR-AMCP-NPC Good Practice Task Force report. *Value Health*. 2014 Mar;17(2):174-82.; Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, Kuntz KM, Meltzer DO, Owens DK, Prosser LA, Salomon JA, Sculpher MJ, Trikalinos TA, Russell LB, Siegel JE, Ganiats TG. Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses: Second Panel on Cost-Effectiveness in Health and Medicine. *JAMA*. 2016 Sep 13;316(10):1093-103.

³⁰ AHRQ. Developing a Protocol for Observational Comparative Effectiveness Research: A User's Guide. Content last reviewed March 2021. Effective Health Care Program, Agency for Healthcare Research and Quality, Rockville, MD. <https://effectivehealthcare.ahrq.gov/products/observational-cer-protocol>

³¹ AHRQ. Developing a Protocol for Observational Comparative Effectiveness Research: A User's Guide. Content last reviewed March 2021. Effective Health Care Program, Agency for Healthcare Research and Quality, Rockville, MD. <https://effectivehealthcare.ahrq.gov/products/observational-cer-protocol>

therapeutic alternatives from potential comparators with the same treatment modality, class, and mechanism of action.

Furthermore, NPC encourages CMS to consult not only current disease-specific clinical guidelines created by physicians and peer-reviewed studies to identify potential therapeutic alternatives but also solicit input from clinicians with expertise in the disease or indication being considered, manufacturers, and patients. Guidelines are a very useful source of information, yet CMS should ensure the guidelines are up-to-date and incorporate the latest evidence.³² CMS should also consider the use of market share data, comparative effectiveness studies and real-world evidence to support the selection of therapeutic alternative.

NPC cautions against using cost to determine a selected drug's therapeutic alternative(s). Rather, during selection of therapeutic alternatives, we encourage CMS to:

- Publicly communicate proposed therapeutic alternatives and permit feedback from manufacturers, clinicians with specific expertise in the treating the disease, patients and caregivers, and other stakeholders before proceeding with comparative effectiveness analyses that inform the initial offer.
- Include patient preferences and priorities that inform shared decision-making between appropriate treatment options.³³
- Invite manufacturers to proactively present clinical information focused on the relative clinical benefit of their products compared to therapeutic alternatives during the process of comparator selection and give manufacturers the opportunity to respond to CMS' choices of therapeutic alternatives (which would also require advanced notice from CMS on which alternatives they will consider). Broad stakeholder engagement, including opportunities for technical input throughout the assessment and clear rules for manufacturer communication of evidence, have been identified as important steps in high-quality value assessment.³⁴ Early manufacturer communication is also consistent with practices employed by state Medicaid agencies, other federal agencies and commercial payers.
- Seek input from clinicians with specific expertise in treating the indication of the selected drug to define appropriate therapeutic alternatives among Medicare patient sub-populations, including patients with multiple comorbidities and varying levels of disease severity.³⁵ There is a long history of guidance to gain this information,³⁶ and

³² National Health Council. A Dialogue on Patient-Centered Value Assessment: Overcoming Barriers to Amplify the Patient Voice. December 2018. Available from: <https://www.nationalhealthcouncil.org/dialogue-patient-centered-value-assessmentovercoming-barriers-amplify-patient-voice>

³³ Schmidt T, Valuck T, Riposo J, et al. Impact of Shared Decision-Making and Patient Decision Aids on Health Care Cost and Utilization in the US: A Systematic Review. *J Clin Pathways*. 2022;8(8):33-43. doi:10.25270/jcp.2022.12.0

³⁴ Sorenson C, Lavezzari G, Daniel G, Burkholder R, Boutin M, Pezalla E, Sanders G, McClellan M. Advancing Value Assessment in the United States: A Multistakeholder Perspective. *Value Health*. 2017 Feb;20(2):299-307. doi: 10.1016/j.jval.2016.11.030.

³⁵ Drummond M, Schwartz JS, Jansson B, Luce BR, Neumann BR, Seibert U, Sullivan SD. Key Principles for the Improved Conduct of Health Technology Assessments for Resource Allocation Decisions. *International Journal of Technology Assessment in Health Care*. 2008. 24:3:250.; Luce BR, Drummond MF, Dubois RW, Neumann PJ, Jönsson B, Siebert U, Schwartz JS. Principles for planning and conducting comparative effectiveness research. *J Comp Eff Res*. 2012 Sep;1(5):431-40

³⁶ Shekelle PG, Woolf SH, Eccles M, Grimshaw J. Clinical guidelines: developing guidelines. *BMJ*. 1999 Feb 27;318(7183):593-6.

NIH's National Center for Advancing Translational Sciences provides tools to help elicit valuable information from practicing clinicians.³⁷

- Limit the choice of therapeutic alternative to drugs and biologics with FDA-approved indications and exclude off-label use from being compared to FDA-approved indications of selected drugs.

C. Prioritize Patient and Caregiver Input

Patients' and caregivers' view of the drugs they take and the benefits they receive is essential to understanding "the full range of clinical and patient-centered outcomes",³⁸ as PCORI stated in their recent multi-stakeholder research initiative. The centrality of direct patient input is echoed in best practices for comparative effectiveness research and value assessment that underpin the concept that the price of pharmaceuticals should be based on the value they provide to patients, caregivers, healthcare systems, and society. Value encompasses the balance of benefits and costs experienced by patients and society over time. There are a multitude of specific benefits that constitute "value," from reducing mortality and improving patient functioning, quality of life, and productivity to outcome equity and societal value of scientific innovation, among others.³⁹

Measures of "indirect costs" such as patient productivity, caregiver time, and treatment burden (such as travel times for repeated hospitalization) are very important to patients and their families but are often poorly captured in administrative claims databases. This misalignment between patient concerns and priorities surrounding the impact of a disease or its treatment and the outcomes data collected in research and care is well documented.⁴⁰ As stewards of the Medicare program accountable to the health of people with Medicare, CMS should include these issues throughout discussions with patients and patient groups and seek and utilize observational studies or real-world evidence that includes these outcomes.

Systematically and rigorously incorporating patient perspectives on the value of selected drugs is essential to ensure that patients have a voice in decisions that affect their health and wellbeing.⁴¹ We are mindful of the federal prohibition on CMS's use of QALYs in coverage and reimbursement decisions. We also emphasize that direct engagement with patients identifies the measures of treatment benefit that patients and their families value, and therefore can avoid the potentially discriminatory nature of aggregate and limited measures such as the QALY. Thus, CMS should take tangible steps to capture the patient voice with validity and

³⁷ NIH National Center for Advancing Translational Sciences. Toolkit for Creating Clinical Care Guidelines: <https://toolkit.ncats.nih.gov/module/after-fda-approval/creating-clinical-care-guidelines/guideline-development-process/>

³⁸ Patient-Centered Outcomes Research Institute (PCORI). Landscape Review and Summary of Patient and Stakeholder Perspectives on Value in Health and Health Care. <https://www.pcori.org/resources/landscape-review-and-summary-patient-and-stakeholder-perspectives-value-health-and-health-care>

³⁹ Neumann PJ, Garrison LP, Willke RJ. The History and Future of the "ISPOR Value Flower": Addressing Limitations of Conventional Cost-Effectiveness Analysis. *Value Health*. 2022 Apr;25(4):558-565.

⁴⁰ Peretto, E.M., Oehrlein, E.M., Love, T.R. et al. Patient-Centered Core Impact Sets: What They are and Why We Need Them. *Patient 15*, 619–627 (2022). <https://doi.org/10.1007/s40271-022-00583-x>

⁴¹ Oortwijn W, Husereau D, Abelson J, et al. Designing and Implementing Deliberative Processes for Health Technology Assessment: A Good Practices Report of a Joint HTAi/ISPOR Task Force. *Int J Technol Assess Health Care*. 2022;38(1).

fidelity, engaging with patient groups directly to understand their perspective on the value of different pharmaceuticals at the following stages of the negotiation process:

1. Defining Unmet Need

The Guidance states that CMS intends to define unmet medical need “as treating a disease or condition in cases where very limited or no other treatment options exist.” This definition is substantially narrower than definitions of unmet need found in the peer-reviewed literature and promulgated by FDA as well as international agencies.

First, the CMS definition incorporates only one of ten elements of unmet medical need identified in a published scoping review (i.e., number of available treatments), an approach considered inadequate in published multi-stakeholder discussions.⁴² The CMS definition of unmet need excludes remaining morbidity from alternative treatments, severity and burden of the disease, and size of the population, among other elements; by excluding treatments that address remaining morbidity from alternative treatments from the definition of unmet need, CMS ignores the considerable value of incremental innovation to patients.

Second, it significantly narrows FDA’s definition of unmet need, as outlined in its guidance for expedited programs. The FDA includes in its definition of unmet need improved efficacy, reduced toxicity and/or potential drug-drug interactions, and improvements in other benefits such as adherence.⁴³ Notably, the FDA definition of unmet need also highlights conditions for which there is significant heterogeneity in response to existing treatment options. Patients may respond differently to available treatment options due to pharmacologic differences, genetic risk, or social determinants of health, creating unmet need despite existing treatments.⁴⁴

Finally, the CMS definition is even narrower than some international practices, which often evaluate unmet need in the context of broader concepts of novelty. These novel considerations include new methods of administration and dosing schedules as well as provision of benefits not captured in conventional measures of health gain (e.g., caregiver benefit, equity, and patient dignity).⁴⁵

We believe assessments of unmet medical need should go beyond simply identifying the number of treatment alternatives in a therapeutic area and encourage CMS to expand their definition of unmet medical need to include a multifaceted definition informed by the patient perspective. Rigorous methods can be used to elicit consensus from clinician experts and have

⁴² Vreman RA, Heikkinen I, Schuurman A, et al. Unmet Medical Need: An Introduction to Definitions and Stakeholder Perceptions. *Value in Health*. 2019;22(11):1275-1282. doi:10.1016/j.jval.2019.07.007

⁴³ Food and Drug Administration. Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. U.S. Department of Health and Human Services. May 2014. Silver Spring, MD. Available at: <https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf>

⁴⁴ National Pharmaceutical Council. The Myth of Average: Why Individual Patient Differences Matter. 2022. Washington, DC. Available at: https://www.npcnow.org/sites/default/files/2022-01/The_Myth_of_Average_01.2022.pdf

⁴⁵ Synnott PG, Voehler D, Enright DE, Kowal S, Ollendorf DA. The Value of New: Consideration of Product Novelty in Health Technology Assessments of Pharmaceuticals. *Appl Health Econ Health Policy*. 2023 Mar;21(2):305-314. doi: 10.1007/s40258-022-00779-0. Epub 2022 Dec 19. PMID: 36529826

been used to identify unmet medical needs to achieve optimal treatment goals throughout the natural history of a disease.⁴⁶ These methods have identified patient-centered unmet needs, including patient quality of life, poor adherence, severe stages of a disease that are hard to treat, and patient preferred routes of administration.⁴⁷ Failure to capture the value of treatments that address patient-centered unmet needs disincentivizes innovations that meet those needs, in turn exacerbating disparities in health outcomes among patients receiving treatments less effective in their subgroups and/or unaligned with their preferences.

2. Selecting alternatives

As discussed above, the choice of comparator is the fundamental driver of any value assessment and its implications for patients and caregivers. Accordingly, patient preferences and priorities that inform shared decision-making between appropriate treatment options should be incorporated into CMS's process for selecting treatment alternatives.⁴⁸ Prioritizing the patient voice in defining unmet medical need promotes patient access to not only *any* treatment alternative but *satisfactory* and *appropriate* treatment options aligned with patient preferences.⁴⁹

3. Determining clinical benefit

We encourage CMS to make use of resources to capture the patient's voice when selecting outcomes for evaluation of relative clinical benefit and to emphasize patient-centered benefits throughout its evaluation process. People with Medicare may prioritize different outcomes, such as symptom relief, improved quality of life, or indirect benefits such as caregiver burden, compared to clinical outcomes like survival or disease progression.⁵⁰ Subgroups of people with Medicare may also have different priorities. Our research has identified heterogeneous patient preferences for both treatment characteristics and outcomes,⁵¹ demonstrating the benefits associated with novel drugs and formulations that provide patients and providers with preference-aligned treatment options. Accordingly, patient preferences regarding the benefits and risks of a product, its available dosage forms, and any innovative delivery systems should be included early in the assessment. Patient preference information can inform many aspects of evaluation of benefit in value assessment, including defining what benefits are most important to patients, selecting measures to quantify benefits, and supplementing health state

⁴⁶ Danese S, Allez M, Van Bodegraven AA, et al. Unmet Medical Needs in Ulcerative Colitis: An Expert Group Consensus. *Digestive Diseases*. 2019;37(4):266-283. doi:10.1159/000496739

⁴⁷ Danese S, Allez M, Van Bodegraven AA, et al. Unmet Medical Needs in Ulcerative Colitis: An Expert Group Consensus. *Digestive Diseases*. 2019;37(4):266-283. doi:10.1159/000496739

⁴⁸ Schmidt T, Valuck T, Riposo J, et al. Impact of Shared Decision-Making and Patient Decision Aids on Health Care Cost and Utilization in the US: A Systematic Review. *J Clin Pathways*. 2022;8(8):33-43. doi:10.25270/jcp.2022.12.0

⁴⁹ Zhang K, Kumar G, Skedgel C. Towards a New Understanding of Unmet Medical Need. *Appl Health Econ Health Policy*. 2021;19(6):785-788. doi:10.1007/s40258-021-00655-3

⁵⁰ Ciarametaro M, Buelt L, Dubois RW. Getting Value Right: The Case For Indirect Benefits. Published online 2020. doi:10.1377/forefront.20200310.267867

⁵¹ Hollin IL, González JM, Buelt L, Ciarametaro M, Dubois RW. Do Patient Preferences Align With Value Frameworks? A Discrete-Choice Experiment of Patients With Breast Cancer. *MDM Policy & Practice*. 2020;5(1). doi:10.1177/2381468320928012

utilities.⁵² The FDA has created useful backgrounders and issued guidance on collection and use of patient preference information.⁵³

In evaluating relative clinical benefit, we encourage CMS to consider patient-reported outcomes that are complete, comprehensive, and fit for purpose, as opposed to limited, QALY utility-based approaches, including QALYs in or outside of a life-extension context.⁵⁴ Fit-for-purpose tools may include disease-specific measures in addition to overarching measures, as well as other outcomes that are meaningful to patients, including productivity, treatment and caregiver burden, and downstream healthcare utilization. Societal benefits, including scientific spillover, limiting the fear and risk of contagion for infectious diseases, and increasing equity have also been recognized as important elements of value.⁵⁵

Comprehensive approaches to measuring patient-centered value, including incorporation of factors beyond effectiveness and side effects, will result in more meaningful comparisons.⁵⁶ Multi-criteria decision analysis (MCDA) is widely recognized and accepted methodology to aggregating different dimensions of value for patient-centered value assessment.⁵⁷ Importantly, MCDA addresses many of concerns of discrimination against disabled and elderly patient that are inherent in utility-based QALYs. While MCDA has important advantages over CEA and other non-consensus methods, it is simply one input to payer decision-making.

CMS has a longstanding commitment to beneficiary engagement. By engaging with patients through surveys, advisory panels, and other forms of direct engagement, CMS can ensure that they are receiving comprehensive and representative information directly from patients to better inform CMS evaluations. We also encourage CMS to emphasize its commitment to patient engagement by including, in its initial offer and price justification, how the patient experience was considered in the evaluation of unmet need, selection of treatment alternatives, and evaluation of clinical benefit.

⁵² Marsh K, de Bekker-Grob E, Cook N, Collacott H, Danyliv A. How to integrate evidence from patient preference studies into health technology assessment: a critical review and recommendations. *International Journal of Technology Assessment in Health Care*. 2021;37(1).

⁵³ FDA. Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities Questions and Answers Guidance for Industry and Review Staff.; 2018. Available at: <https://www.fda.gov/media/133620/download>

⁵⁴ Brown J, Cryer DR. Is the QALY Fit for Purpose? *Am J Accountable Care*. 2021;9(2):8-13.

⁵⁵ Lakdawalla DN, Doshi JA, Garrison LP Jr, Phelps CE, Basu A, Danzon PM. Defining Elements of Value in Health Care-A Health Economics Approach: An ISPOR Special Task Force Report [3]. *Value Health*. 2018 Feb;21(2):131-139. doi: 10.1016/j.jval.2017.12.007.

⁵⁶ Westrich K, Lisabeth Buelt M. *Current Landscape: Value Assessment Frameworks*. Washington, DC: National Pharmaceutical Council; 2016.

⁵⁷ National Pharmaceutical Council. *Multi-Criteria Decision Analysis: Can It Help Make Value Assessment More Patient Centered?* 2020. Washington, DC. Available at: <https://www.npcnow.org/sites/default/files/media/2020mcda-roundtable-nhc-npc-whitepaper-final.pdf>; Mendola ND, Oehrlein E, Perfetto EM, Westrich K, McQueen RB. Stakeholder perception of pharmaceutical value: A multicriteria decision analysis pilot case study for value assessment in the United States. *J Manag Care Spec Pharm*. 2022 Oct;28(10):1190-1196.

II. (Section 110) Part D Formulary Inclusion of Selected Drugs

The IRA requires Part D plan sponsors to include on their formularies drugs for which an MFP is available. However, the perverse incentives that remain in the ecosystem could be exacerbated because the MFP process will occur concurrently with Part D redesign; more so if selected drugs are in competitive classes and may be priced below the ceiling price. This could lead to adverse tiering impacting patient copayments and/or formulary-driven switching, increased utilization management, or other reductions in beneficiary access thwarting the intent of the MFP process and undermining the competition that has made Medicare Part D a success.

Experts have already warned that the intersection of MFP and Part D redesign provisions are likely to increase formulary exclusions.⁵⁸ CMS should provide additional guidance about how to ensure selected and non-selected treatments are included in Part D formularies. CMS should also consider the risk of Medicare Prescription Drug Plans (PDPs) penalizing selected drugs compared to non-selected drugs in the same therapeutic class with adverse tiering or overly burdensome utilization management. CMS should also redefine Part D negotiated price to include all manufacturer price concessions, which would put less pressure on plan sponsors in the catastrophic phase of the benefit and decrease beneficiary coinsurance for both selected and non-selected drugs.

NPC and others will be closely monitoring changes to patient access as a result of IRA and encourages the agency to pay close attention to decreased access or discriminatory behavior.

III. General Comments

A. Adjusting the preliminary price downward for existing patents and exclusivities

In section 60.3.4, Consideration of Manufacturer-Specific Data, the Guidance specifies that the agency intends to “*consider the length of the available patents and exclusivities before the selected drug may no longer be single source. For example, if the selected drug has patents and exclusivities that will last for a number of years, CMS may consider adjusting the preliminary price downward.*” The IRA statute establishes an applicable percentage of non-FAMP ceiling price based on the length of time since a selected drug was approved. Because that formula already factors in historical exclusivity periods, adjusting the price downward represents a double counting not expressly permitted in the statute.

NPC disagrees with CMS’ proposal to adjust the preliminary price downward for selected drugs that have existing patents and exclusivities, including Orphan Drug Exclusivity and Pediatric Exclusivity. Patents and regulatory exclusivity are critical mechanisms to accelerate innovation and incentivize research and development for both existing and emerging products, particularly

⁵⁸ Kelly C. Medicare Part D Redesign Could Expand Rebate-Driven Formulary Exclusions in Program. The Pink Sheet. January 26, 2023. <https://pink.pharmaintelligence.informa.com/PS147634/Medicare-Part-D-Redesign-Could-Expand-Rebate-Driven-Formulary-Exclusions-In-Program>

when addressing unmet needs in orphan and pediatric populations.⁵⁹ Accordingly, this proposal will hinder innovation in areas where vital momentum to develop clinically important therapies has increased over time.

Orphan drug development has accelerated over the past four decades, resulting in more novel treatments for patients with rare diseases, particularly in the therapeutic areas of oncology, neurology, and infectious disease.⁶⁰ Pediatric research has also grown considerably, with nearly all drugs granted exclusivity for pediatric research receiving new pediatric labeling, most often a new or expanded pediatric indication.⁶¹

B. Orphan drug development

Though CMS published Section 30 of the guidance as final, we are encouraged that the agency *“is considering whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development.”* People with rare diseases face significantly higher health care costs,⁶² and these patients and their families highly value the current and future treatments that meet their needs. Furthermore, the small patient populations for which orphan drugs are indicated are highly sensitive to changes in the research and development landscape, and the companies that develop orphan drugs are additionally highly sensitive to changes in the reimbursement landscape – especially those that threaten their ability to bring new orphan treatment to market and conduct post-approval research and development.

As such, we encourage CMS to broadly interpret the discretion provided by the IRA statute to exclude orphan drugs from negotiation and when determining the number of designations and indications that exempt an orphan product from selection. For example,

- CMS should incorporate the definition in the Orphan Drug Act and exclude from negotiation a drug intended to treat a condition affecting fewer than 200,000 persons in the United States. CMS’s too-narrow orphan drug exclusion jeopardizes the development of rare disease therapies that treat fewer than 200,000 patients across multiple indications.
- CMS should support orphan drug development by clarifying that for orphan drugs the 7- or 11-year period that must elapse before a drug can be considered for negotiation begins upon the date that the orphan drug exclusion no longer applies.

⁵⁹ Grabowski HG, DiMasi JA, Long G. The roles of patents and research and development incentives in biopharmaceutical innovation. *Health Aff (Millwood)*. 2015 Feb;34(2):302-10. doi: 10.1377/hlthaff.2014.1047.

⁶⁰ Miller, K.L., Fermaglich, L.J. & Maynard, J. Using four decades of FDA orphan drug designations to describe trends in rare disease drug development: substantial growth seen in development of drugs for rare oncologic, neurologic, and pediatric-onset diseases. *Orphanet J Rare Dis* **16**, 265 (2021). <https://doi.org/10.1186/s13023-021-01901-6>

⁶¹ Wharton GT, Murphy MD, Avant D, et al. Impact of Pediatric Exclusivity on Drug Labeling and Demonstrations of Efficacy. *Pediatrics* 2014 Aug;134(2):e512-8. doi: 10.1542/peds.2013-2987. Epub 2014 Jul 14

⁶² Tisdale, A., Cutillo, C.M., Nathan, R. *et al.* The IDeaS initiative: pilot study to assess the impact of rare diseases on patients and healthcare systems. *Orphanet J Rare Dis* **16**, 429 (2021). <https://doi.org/10.1186/s13023-021-02061-3>

C. Application of MFP across dosage forms and strengths

NPC appreciates that CMS is seeking comments under section 60.5 on approaches to the application of the MFP across dosage forms and strengths that could accurately and fairly compensate manufacturers and other entities. As stated earlier in this document, our research demonstrates how novel formulations provide patients and providers with treatment options that account for heterogeneous patient preferences⁶³ and promote medication adherence through reduced regimen complexity.⁶⁴ Given the documented value of dosage form innovation on patient-centered care and outcomes, NPC encourages CMS to incorporate the value of novel formulations in its price determination and negotiation process.


We also recommend that CMS provide more clarity in the calculation of 30-day equivalent supplies. The use of loading doses, weight-based dosing, and severity-based dosing are common clinical practices that result in the amount of medicine being used by one patient being different than that used by others. This is yet another reason why CMS should consult with manufacturers early and often in its process, and openly communicate important information such as the agency's estimation of a 30-day equivalent supply and how that compares with actual use across the Medicare population.

NPC is disappointed that CMS chose a broad and sweeping approach to defining qualifying single-source drugs in Section 30 and did not invite stakeholder feedback on that process. The definition ignores the value of novel formulations and delivery systems, which should be considered at the selection phase of the process not the MFP application phase.

IV. Conclusion

The National Pharmaceutical Council appreciates the opportunity to submit comments in response to this Guidance and looks forward to additional opportunities to engage with CMS as it implements the Medicare Drug Price Negotiation Program. Please contact me at john.obrien@npcnow.org or (202) 827-2080 if we may provide any additional information.

Sincerely,



John Michael O'Brien, PharmD, MPH
President & Chief Executive Officer

⁶³ Hollin IL, González JM, Buelt L, Ciarametaro M, Dubois RW. Do Patient Preferences Align With Value Frameworks? A Discrete-Choice Experiment of Patients With Breast Cancer. *MDM Policy & Practice*. 2020;5(1). doi:[10.1177/2381468320928012](https://doi.org/10.1177/2381468320928012)

⁶⁴ Wertheimer AI, Santella TM, Finestone AJ, Levy RA. Drug delivery systems improve pharmaceutical profile and facilitate medication adherence. *Adv Ther*. 2005 Nov-Dec;22(6):559-77. doi: 10.1007/BF02849950.



Our Mission: To drive efforts to cure psoriatic disease and improve the lives of those affected.

April 14, 2023

Meena Seshamani, M.D., Ph.D.,
Deputy Administrator, Centers for Medicare & Medicaid Services
Director of the Center for Medicare
Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-1850

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Deputy Administrator Seshamani,

Thank you for the opportunity to provide comment on the guidance for the Medicare Drug Price Negotiation Program (Program) for initial price applicability year 2026. I write on behalf of the National Psoriasis Foundation (NPF) to submit feedback on the initial guidance. In addition, we encourage the Centers for Medicare & Medicaid Service (CMS) to design the Program to ensure it improves patient access as well as treatment affordability.

Psoriatic disease is a heterogeneous, immune-mediated condition that affects over eight million Americans. While psoriatic disease primarily affects the skin, most patients have evidence of systemic inflammation which increases their risk for the development of many comorbidities. For example, approximately one-third of psoriasis patients have or will go on to develop psoriatic arthritis with severe pain and/or irreversible bone loss. Psoriatic disease is also associated with several co-occurring conditions such as cardiovascular disease including stroke and hypertension, diabetes, metabolic syndrome, depression/anxiety, and cancer.

Patients living with psoriatic disease need consistent and timely access to treatment to reduce symptoms and mitigate the harmful systemic effects of this condition. Treatments include prescription topical therapies, UV-based light therapy, oral medicines, and biologics.

For over 55 years, the NPF has been the leading advocacy voice in the effort to cure psoriatic disease and improve the lives of those affected. The NPF supports the psoriatic disease community through state and federal advocacy efforts, provider and patient education, patient support, research, and the development of treatment recommendations and guidelines. We are also committed to supporting the work of government and policymakers to address and advance solutions to improve health outcomes for individuals living with chronic disease.

Utilization Management

As CMS develops the Medicare Drug Price Negotiation Program, NPF urges CMS to evaluate policy decisions based on how it will affect patient access to needed treatments. The NPF urges CMS to consider our [position statement on access to care](#) as this process develops. For example, formulary design may change, which could lead to utilization management protocols that destabilize patients with ongoing treatment or further delay access to needed prescriptions. CMS should go above and beyond to establish guardrails in the implementation of the Program to ensure that patient treatment plans are not negatively affected.

In addition, between now and 2026, NPF encourages CMS to:

- Assess the current impact of utilization management, including prior authorization and step therapy, on patient access to prescription drugs as well as health outcomes
- Ensure that existing guardrails are working, such as the step therapy exceptions process and prohibiting step therapy for treatments that patients are stable on
- Consider additional patient protections that could ensure appropriate and timely access, such as extending the prohibition of step therapy for stable patients to Part D

Finally, NPF encourages CMS to monitor and report on whether utilization management like prior authorization and step therapy increased/decreased as a result of the Program, and how timely patient access to prescriptions was affected.

Patient Engagement and Value Assessment

Engaging the patient community to understand the perspectives of people living with chronic diseases and disabilities is vital to the success of IRA implementation. The NPF has long been a leader in engaging our community to [best understand their perspectives](#) on the development of a treatment and in the [health technology assessment/value](#) conversation.

We appreciate CMS stating that it will not use metrics such as QALYs. All individuals living with chronic diseases deserve to be treated equally regardless of age, disability status, or other special populations. The NPF joins others in our community to express concern over the external data submission timing. Thirty days to submit data after release of the list of drugs to be negotiated is a significant challenge and is likely to present a challenge in truly assessing the value of a treatment. We believe CMS should extend the timeframe for stakeholders to submit requested data or provide additional opportunities in the process to accept data from the patient community.

Section 30.3 – Selection of Drugs for Negotiation for Initial Price Applicability Year 2026

NPF appreciates that the outlined policies related to biosimilars closely match the statute. Where CMS has flexibility, we encourage CMS to favor policies that support a robust biosimilars market that drives down prices for patients. We encourage CMS to consider any unintended consequences that may hinder a robust biosimilars market or that disincentive the development of biosimilars.

Section 50 – Negotiation Factors

NPF applauds CMS for allowing the public, including patients, to submit data for the Negotiation Data Elements Information Collection Request (ICR). In addition, we encourage CMS to consider additional ways to engage the patient community as it collects information to support negotiating the maximum fair price. For example, opportunities for patients to provide live testimony have been impactful in other government decision related to access to care.

Section 60 – Negotiation Process

When reviewing therapeutic alternatives, please consider the following:

- It is important for patient communities to have access to a broad array of treatment options. Each patient is unique in the way they respond to therapy, and there is no ‘one size fits all’ approach.
- Stable patients should not be switched to different treatments, unless prescribed by their physician or where the alternative is a generic or biosimilar. Switching patients may destabilize their health, and patients may develop immunogenicity to the treatment that was working for them. It is critical to ensure the treating physician and patient are informed of any switches with ample time to appeal as necessary.
- Stable patients should not be exposed to increased drug cost sharing because they were unwilling to switch treatments.

When reviewing clinical efficacy, please consider the following:

- The drug’s delivery mechanism can significantly impact treatment adherence and patient quality of life.
- NPF applauds CMS for considering patient reported outcomes (PROs) and encourages CMS to deepen its engagement with patient communities to ensure adequate communication of PROs.

Section 90.2 – Monitoring Access to the Maximum Fair Price

NPF agrees that patient cost-sharing should be based on the MFP. If a lower price is negotiated via rebates or other mechanisms, then the cost sharing should be based on the lowest price.

To help ensure that MFP-eligible communities have access to the MFP, CMS should include the MFP in the plan holder’s statement of benefits. This would enable the beneficiary to confirm whether their cost-sharing was based on the MFP. In addition, to illustrate the direct impact of the Program for beneficiaries, CMS could include information on how the MFP compares to the drug price prior to inclusion in the Program.

Conclusion

Thank you for your consideration of our views on the initial guidance for the Drug Price Negotiation Program. We hope for the opportunity to continue to engage with CMS via comments as well as in person meetings as the agency implements the prescription drug provisions of the Inflation Reduction Act. For additional information, please contact Sarah Buchanan, Director of Government Relations and Health Policy, at sbuchanan@psoriasis.org.

Sincerely,

A handwritten signature in black ink, appearing to read "Jason Harris". The signature is fluid and cursive, with the first name "Jason" being more prominent than the last name "Harris".

Jason Harris
Vice President, Government Relations & Advocacy
National Psoriasis Foundation



Submitted April 14, 2023
Sent via Electronic Mail

Dr. Meena Seshamani, M.D., Ph.D., CMS Deputy Administrator and Director of the Center for Medicare Center for Medicare and Medicaid Services

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Dr. Seshamani,

The National Council for Prescription Drug Programs (NCPDP) is a not-for-profit American National Standards Institute (ANSI) accredited Standards Developer (ASD) consisting of more than 1,500 members representing entities including, but not limited to, claims processors, data management and analysis vendors, federal and state government agencies, insurers, intermediaries, pharmaceutical manufacturers, pharmacies, pharmacy benefit managers, professional services organizations, software and system vendors and other parties interested in electronic standardization within the pharmacy services sector of the healthcare industry. NCPDP provides a forum wherein our diverse membership can develop business solutions, including ANSI-accredited standards and guidance for promoting information exchanges related to medications, supplies and services within the healthcare system.

For over 40 years, NCPDP has been committed to furthering the electronic exchange of information between healthcare stakeholders. The NCPDP Telecommunication Standard is the standard used for eligibility, claims processing, reporting and other functions in the pharmacy services industry as named in Health Insurance Portability and Accountability ACT (HIPAA). The NCPDP SCRIPT Standard and the Formulary and Benefit Standard are the standards in use in electronic prescribing as named in Medicare Modernization Act (MMA).

NCPDP requests an extension for additional comments to the *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments*, released March 15, 2023.

NCPDP additional comments will be submitted no later than May 31, 2023. NCPDP needs additional time to engage the wide range of impacted stakeholders, such as wholesalers, pharmacies, drug data compendia, payers/plans, intermediaries/software vendors, PBMs/processors and providers or pharmacy claim reconciliation services.

The initial NCPDP comments are as follows:

Section 90.2 Monitoring of Access to the MFP

...

“For example, a pharmacy may purchase a medication for \$100 per bottle and the MFP as applied to this selected package is \$80. The Medicare beneficiary is enrolled in a Part D plan under which coverage of the selected drug is available, thus the beneficiary is an MFP-eligible individual. For

this example, the plan has not negotiated a lower price for the medication. The pharmacy provides the negotiated price (i.e., MFP plus a dispensing fee) at the point of sale to the Medicare beneficiary. As a result of this transaction, the pharmacy is owed \$20 by the manufacturer. The pharmacy would submit the information regarding the \$20 chargeback amount to its wholesaler and receive a credit from the wholesaler for that amount. The wholesaler would be compensated by the manufacturer after billing the manufacturer for the chargeback amount.”

NCPDP Comment: There is not a current NCPDP standard to facilitate this requirement. NCPDP would welcome the opportunity to work with impacted industry partners such as CMS, wholesalers and pharmacies to develop a standards solution for the MFP requirements.

Appendix C: Definitions for Purposes of Collecting Manufacturer-Specific Data

Current Unit Costs of Production and Distribution (pages 85-86 and page 89)

“For the purposes of describing current unit costs of production and distribution to be collected for use in the Negotiation Program for the selected drug, as described in section 1194(e)(1) of the Act and section 50.1 of this memorandum, CMS intends to adopt the definitions described in this subsection.

- *In accordance with section 1191(c)(6) of the Act, the term ‘unit’ means, with respect to a drug or biological product, the lowest identifiable amount (such as a capsule or tablet, milligram of molecules, or grams) of the drug or biological product that is dispensed or furnished.*
- *Units must be reported in one of the three National Council for Prescription Drug Programs (NCPDP) Billing Unit Standards (BUS): each (EA), milliliter (ML), or gram (GM). The unit reported must be specified for each of the NDC-9s included in the selected drug. Selections of EA, ML or GM must be made as follows:*
 - *“EA” is used when the product is dispensed in discrete units. These products are not measured by volume or weight. The Billing Unit of “EA” is also used to address exceptions where “GM” and “ML” are not applicable. Examples of products defined as “EA” include, but are not limited to:*
 - *Tablets;*
 - *Capsules;*
 - *Suppositories;*
 - *Transdermal patches;*
 - *Non-filled syringes;*
 - *Tapes;*
 - *Devices/Digital Therapies;*
 - *Blister packs;*
 - *Oral powder packets;*
 - *Powder filled vials for injection;*
 - *Kits; and*
 - *Unit-of-use packages of products other than injectables with a quantity less than one milliliter or gram should be billed as “one each,” for example, ointment in packets of less than 1 gram or eye drops in dropperettes that contain less than 1 mL.*
 - *“ML” is used when a product is measured by its liquid volume. Examples of products defined as “ML” include, but are not limited to:*
 - *Liquid non-injectable products of 1 mL or greater;*
 - *Liquid injectable products in vials/ampules/syringes;*

- *Reconstitutable non-injectable products at the final volume after reconstitution except when they are in powder packets; and*
- *Inhalers (when labeled as milliliters on the product).*
- *“GM” is used when a product is measured by its weight. Examples of products defined as “GM” include, but are not limited to:*
 - *Creams (of 1 GM or greater);*
 - *Ointments (of 1 GM or greater); and*
 - *Inhalers (when labeled as GM on the product.*

NCPDP Comment: NCPDP reviewed this section of the initial memorandum and recommends making an addition to the second bullet, first sub-bullet at the eleventh sub-sub-bullet which states “Kits; and”. Since NCPDP has a specific definition for “Kits” and pharmaceutical manufacturers sometimes have a different view regarding what constitutes a kit, NCPDP recommends adding the following quote from the NCPDP Billing Unit Standard (*NCPDP Billing Unit Standard Implementation Guide Version 4.0 (January 2022), Section 5.5.1, page 14*) to specifically define the term “Kits” as used in this list:

- “Kits are defined as products that contain one of the following:
 - 1) at least two distinct items with different billing units
 - 2) one product packaged with medicated or unmedicated swabs, wipes and/or cotton swabs/balls
 - 3) meters packaged with test strips”

NCPDP understands that CMS used the publicly available *NCPDP BILLING UNIT STANDARD FACT SHEET* (June 2020) as the reference for the list in Appendix C and the “Kits” definition is not included on the Fact Sheet. However, to avoid any possible confusion regarding kits stemming from the initial memorandum, NCPDP recommends this addition.

NCPDP thanks CMS for the consideration of our initial comments and our request for an extension to provide additional comments. NCPDP looks forward to continuing its work with CMS.

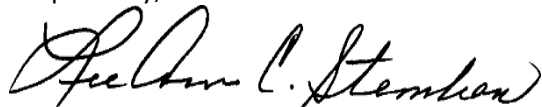
For direct inquiries or questions related to this letter, please contact:

Teresa Strickland

NCPDP Technical Advisor, Standards Development

standards@ncdpd.org

Respectfully,



Lee Ann C. Stember

President & CEO

National Council for Prescription Drug Programs (NCPDP)

April 14, 2023

The Honorable Chiquita Brooks-LaSure, Administrator
Centers for Medicare & Medicaid Services
Hubert H. Humphrey Building Room 445-G
200 Independence Ave, SW
Washington, DC 20201
Delivered electronically via: IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator La-Sure,

Thank you for the opportunity to comment on the “Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026.”

I am writing on behalf of No Patient Left Behind (NPLB), a non-profit organization comprised of biotech investors, innovators, researchers, physicians, and patient advocates dedicated to three guiding principles: 1) prescribed treatments authorized by an insurer should be affordable to patients through zero or low out-of-pocket costs; 2) drug prices should not stay high for too long; and 3) sufficient R&D incentives must remain in place to ensure continued U.S. biotech innovation.

NPLB believes CMS can improve the Inflation Reduction Act (IRA) on behalf of patients, innovators, payors, and society with three proposed modifications. I also hope you review the more detailed [supplemental comments](#) at the end of this letter to assist CMS’ successful implementation of the new law.

Recommendations to improve IRA:

- 1) Small molecule parity.** We urge the administration to work to limit IRA’s harmful impact on new small molecule R&D by initiating negotiation of New Drug Application (NDA) path therapies 13 years after Food and Drug Administration (FDA) approval. NPLB’s presentation, “[How IRA makes new small molecule R&D uninvestable](#)”, lays out in detail with specific examples from development stage biotech CEOs and patient advocates of how IRA’s penalty against new drug application treatments vs. biologics license application treatments (NDAs vs. BLAs) will result in fewer new therapies, particularly a meaningful reduction in oncology treatments. By prioritizing R&D in physician-administered shots over self-administered pills, IRA also will result in higher costs to patients, employers, and the federal government, which likely will miss out on significant future savings and lower out-of-pocket costs achieved through the proven market competition and reliable interchangeability of abbreviated new drug application (ANDAs) “generic” therapies. For Medicare beneficiaries, the IRA incentivizing BLAs over NDAs also means that many future therapies will be covered by Medicare Part B that lacks IRA’s new \$2000 annual catastrophic out-of-pocket cost limit.
- 2) Incorporate Generalized Cost-effectiveness Analysis (GCEA) Methodologies.** When determining the value of an innovative medicine during the price-setting process, CMS should not rely on faulty and outdated math used by foreign governments, the Institute for Clinical and Economic Review (ICER), and vertically integrated U.S. health plans. These entities use traditional CEA math to deny patients access to innovative medicines via lack of coverage or unreasonably high out-of-pocket costs that health economists know deter patient access to prescribed treatments. Traditional CEA models purposefully omit real-world values of medicine impactful to patients, their families, and society. For example, ICER’s faulty and outdated math does not include simple,

demonstrable values, and basic facts, such as that medicines go generic, the likelihood of therapeutic competition, population changes, that caregivers and spouses are liberated and increase productivity when a patient gets better, and that medicines reduce risk for everyone worried about getting sick, incapacitated, or killed by a horrible condition. Furthermore, ICER's outdated methodology stubbornly relies on a 3% discount rate when even the [U.S. Office of Management & Budget is proposing economists use a 1.7% discount rate to determine the future value of innovations](#).

Please take the time to consider incorporating elements from [this updated value "flower"](#) in your health technology assessment calculations. It highlights which limited factors traditional CEAs use, the calculable values that updated CEAs could easily take into account today, and what additional values stakeholders should consider using in the future. The differentiation between traditional CEA and updated GCEA math also is explained [via this brief animation](#).

- 3) Low or no beneficiary cost-sharing for government negotiated drugs:** It is vital that CMS implements the law so that beneficiaries, not vertically integrated health plans and their sister organizations, benefit from a government price negotiation process that effectively transforms patent protected therapies into functionally generic government price set commodities. CMS has both the legislative requirement and strategic expertise in the negotiation process to require Medicare Advantage (MA), MA-PD plans, and Pharmacy Benefit Managers (PBMs) that take advantage of government negotiated prices to meaningfully lower both Part D and Part B beneficiaries' out-of-pocket costs.

Requiring government "negotiated" savings be passed on to beneficiaries in the form of low or no out-of-pocket costs similar to how plans treat generic therapies is necessary to maximize the IRA's benefits to Part D beneficiaries. For example, the Kaiser Family Foundation reported that "[most Part D enrollees pay less than \\$10 for generic drugs, but many pay \\$40-\\$100 \(or coinsurance of 40%-50%\) for brand-name drugs](#)." The IRA will not fulfill both its legislative requirement and intended impact unless CMS contractually assures manufacturers and requires MA plans to similarly limit beneficiary out-of-pocket costs to less than \$10 at Tier 1 copayments for all government negotiated drugs.

Similarly for Part B, while there is a 20% coinsurance limit per service, beneficiaries lack a catastrophic out-of-pocket cost cap. CMS should contractually require purchasers of Part B services that benefit from IRA's new government negotiation process to charge no coinsurance or copayments in order to ensure that beneficiaries see commensurate out-of-pocket savings due to government intervention and price-setting.

Regarding health plan prior authorization requirements, we appreciate CMS' recent efforts to end some of the unethical ways health plans have recently begun to use prior authorization to arbitrarily deny care and make it administratively burdensome for sick patients to access covered prescribed therapies at an affordable cost. Once again, NPLB recommends CMS requires plans use an expedited prior authorization process or prohibit prior authorization altogether for generic and government negotiated drugs.

In conclusion, NPLB supports IRA’s intent to achieve biotech affordability and innovation. We believe CMS and the Administration have an opportunity to help improve IRA so that it 1) treats all innovative therapies fairly at 13 years after FDA approval, 2) improves and updates traditional CEA methodology to help determine a medicine’s true value, and 3) requires MA plans to actually reduce beneficiary out-of-pocket costs for government negotiated drugs equivalent to a plan’s existing lowest-tier generic drug copayment.

Sincerely,

Peter Rubin
Executive Director
No Patient Left Behind (NPLB)
prubin@nopatientleftbehind.org

Supplemental Guidance Comments

Section 30 – Overarching Comment		
It is unfortunate that CMS considers the selection process for drugs for the first year of the program final. It is important that regulators also consider comments to Section 30 knowing that CMS rulemaking can often change or delay before, after, and during a plan year -- particularly when implementing a new program.		
Provision	Concern	Recommendation
(30.1) Medicare negotiation for NDA-path drugs at nine-years post-launch.	Erosion of the R&D case for all NDA-path drugs (small molecules, peptides, oligos, etc.) for diseases of aging. See NPLB’s open letter from leading biotech investors and innovators for a better understanding of how IRA makes new small molecule R&D uninvestable.	CMS should seek parity for NDA-path and BLA-path drugs by initiating government price “negotiation” 13 years after FDA approval. NPLB supports CMS seeking a larger minimum discount as necessary to ensure budget neutrality resulting from an NDA negotiation timing change.
(30.1.1) Orphan drug “exclusion” for only one indication.	Drugs approved for a second orphan indication under a separate ODD will be subject to negotiation. This prevents	The harms from IRA’s treatment of orphan drugs could be mostly alleviated by creating small- and large-molecule parity for

	<p>companies from trying to treat multiple orphan diseases and hampers orphan drug development.</p> <p>This article illustrates how IRA already is reducing orphan drug R&D for patients whose indications have unmet medical needs.</p>	<p>negotiation at 13 years (see above).</p> <p>CMS should look to only active orphan drug designations for the purposes of determining eligibility for the orphan drug exclusion (not including withdrawn orphan drug designations).</p>
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Provision	Concern	Recommendation
<p>(30.1.1) orphan drug exclusion, all dosage forms and strengths and different formulations (active moiety) of the qualifying single source drug described in section 30.1 of this memorandum must meet the criteria for exclusion.</p> <p>[CMS looks to the orphan drug designations (ODDs) of all approved dosage forms, strengths, formulations of a drug (active moiety) and only grants a negotiation exemption if all of them fall under one ODD.]</p> <p>(90.4) For the purposes of determining if a drug can be selected (or should still be subject to negotiation once selected), CMS will look to whether there is an approved generic or biosimilar under 505(j) or 351(k), and also bona fide marketing/robust and meaningful competition of a generic or biosimilar brand.</p> <p>CMS will categorize drugs by</p>	<p>CMS's guidance presents an impediment to drug repurposing that will deprive patients from benefiting from new uses of old medicines that require radically different formulations.</p> <p>NPLB opposes gimmicks used to inappropriately delay generic market entry. However, there are limited cases where innovators see a R&D opportunity to add risk and develop a generic drug in a novel way, in a novel formulation, to treat a new orphan disease that could not possibly be treated using the existing generic (e.g., too toxic or doesn't reach high enough concentrations in the target tissue).</p> <p>To justify funding the development of the new formulation, innovators would count on the orphan exemption (again, because nine years is too short), and yet, the old generic drug, while functionally irrelevant to the treatment of the new disease, would</p>	<p>Ideally, NDA-path drugs would be negotiated 13 years after FDA approval – thus mitigating IRA's harms and the complexity of CMS' rulemaking.</p> <p>Until then, investors and innovators need to know if the old generic drug's approvals serve to invalidate the orphan exemption of the new formulation. CMS then would consider the availability of generics to also serve as a basis for not selecting the new innovative formulation for negotiation (at least not until year 11 for price reduction after 13 years).</p> <p>Furthermore, the bona fide marketing standard is extra-statutory in nature with no basis in the law, which defines the standard simply as "marketed". The standard is ambiguous and subjective. The appropriate test, as specified in the IRA, is an objective, point-in-time determination of whether a drug has been "marketed," which can be determined by reference to the "market date"</p>

<p>active moiety to determine eligibility for negotiation.</p>	<p>invalidate the new formulation's orphan exemption, deterring investment in its development.</p> <p>However, the presence of the generics could also serve as a basis for the moiety in all its forms (including the new formulation) to not be selected for negotiation, which investors would find reassuring for their funding of the new formulation. In practical contradiction, CMS' guidance suggests it may apply its arbitrary standard to determine that the original generic is not "bona fide" competition, thus making the new drug eligible for Medicare price negotiation at nine years, thereby deterring investment in its development.</p>	<p>reported by the manufacturer to the Medicaid Drug Rebate Program. It is defined as the date on which the drug is first sold in the US, and is the standard that CMS is using to determine whether a drug is marketed for purposes of the MDRP, the Part D inflation rebate guidance, and ASP (where the standard is articulated slightly different as the "first sale date."</p>
<p>Other sections</p>		
Provision	Concern	Recommendation
<p>(50.2) CMS' processes for determining the Maximum Fair Price for individual medicines as well as the relevance of "therapeutic alternatives" to the drugs it selects for negotiation.</p>	<p>Cost-effectiveness math embraced by ICER in the US and other HTA bodies elsewhere (e.g., NICE in the UK) is so simplified that it excludes many demonstrable benefits of medicines (e.g., they liberate caregivers, they reduce risk for healthy people, they go generic yet keep on working), resulting in extreme under-estimations of the value of new medicines. This math can then serve as an excuse for plans to refuse coverage, essentially telling patients that the medicines aren't worth their prices instead of admitting that the plan just doesn't want to cover or reimburse for the prescribed</p>	<p>To the extent that CMS wants to appreciate the value that a medicine brings to society before it decides how aggressively to set its price (particularly in the case of NDA-path drugs that experience negotiation far sooner than would have gone generic), CMS should broadly account for a medicine's value element, using a dynamic stacked cohort model that accounts for value to patients, to caregivers, and to the rest of the population whose risk is reduced by having the drug (i.e., if it's going to do CEA, do generalized CEA, not conventional over-simplified CEA).</p>

	<p>treatment.</p> <p>Considering that drugs can go generic and keep us out of hospitals and nursing homes, which do not go generic. ICER-like over-simplified CEA math that undervalues drugs would signal to investors and innovators that the value of new medicines will be willfully underestimated to justify not rewarding their development, which will turn investors away from funding future biomedical R&D.</p>	<p>CMS should consider key product attributes like efficacy, safety, and ease-of-use in determining relevant "therapeutic alternatives" (the basis for CMS' opening bid).</p>
Provision	Concern	Recommendation
<p>(90.4) For the purposes of determining if a drug can be selected (or should still be subject to negotiation once selected), CMS will look to whether there is an approved generic or biosimilar under 505(j) or 351(k), and also bona fide marketing/robust and meaningful competition of a generic or biosimilar brand.</p> <p>CMS will categorize drugs by active moiety to determine eligibility for negotiation.</p>	<p>CMS' broad discretion in determining what is "bona fide competition" suggests it favors the ability to determine drug price via its negotiation process rather than letting true competition play out in the marketplace.</p> <p>The "bona fide" generic competition standard will reduce the reward for first filer generics and hurt generic competition.</p> <p>Nowhere does the guidance specify what share or availability metrics may qualify as "bona fide."</p> <p>CMS is basically looking to the slowest adopters of generics (part D plans) to determine if competition is real.</p>	<p>The IRA threatens to make generic business models unsustainable for drugs that treat Medicare populations. One might think this does not matter because price reduction will be achieved via negotiation. However, because generic competition often drives costs down not only by eroding the gross margins of the original drug but also spurring manufacturing improvements that lower cost of goods, the IRA threatens to leave society paying more for old drugs in the long run by deterring generic competition.</p> <p>This could increase overall costs across market segments (Medicare and commercial payers).</p>

<p>(40.2.2) CMS prohibitions on data disclosure and destruction of related documents.</p>	<p>The lack of transparency around the negotiation process makes it impossible for companies to understand which value components CMS is measuring in determining MFP.</p>	<p>CMS’s process for determining value and cost-effectiveness should be transparent (vs. gag order and document destruction that they propose today). It should be able to defend what it considers to be a “fair price.”</p> <p>Furthermore, this prohibition violates company First Amendment rights. Companies subject to the negotiation process need to be able to disclose to their boards and their investors what occurred in the negotiation process.</p>
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April 14, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator, Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building, Room 445-G
200 Independence Avenue, SW
Washington DC 20201

Re: Medicare Drug Price Negotiation Program Proposed Guidance: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Brooks-LaSure,

Novartis Services, Inc. submits this letter on behalf of Novartis Pharmaceuticals Corporation and its affiliates referred to collectively herein as “Novartis” and appreciates the opportunity to comment on the initial guidance regarding the Drug Price Negotiation Program (“Negotiation Program”) issued by the Centers for Medicare & Medicaid Services (“CMS”) on March 15, 2023 (“Initial Guidance”).¹

Novartis provides health care solutions that address the evolving needs of patients and societies worldwide. We are a focused medicines company concentrated on the core therapeutic areas of cardiovascular, immunology, neuroscience, solid tumors, and hematology. At Novartis, we are united by a single purpose to reimagine medicine to improve and extend lives. Through innovative science and technology, we address some of society’s most challenging health care issues. We work to discover and develop breakthrough treatments and find new ways to deliver them to as many people as possible. Our vision is to be the most valued and trusted medicines company in the world.

Novartis remains concerned that the Negotiation Program, as prescribed by the Inflation Reduction Act (“IRA”), will have profoundly detrimental effects on the development of innovative medicines in the U.S. The program is not structured as a negotiation, akin to the market-based negotiations that occur in Medicare Part D today, but rather as a blunt price setting tool arbitrarily applied to innovative medicines after a certain number of years on the market. The far-reaching consequences of the IRA go well beyond impacts to the Medicare program and risk threatening the innovation ecosystem that has brought life-changing medicines to the U.S. market. Over just the past six years, Novartis is proud to have advanced ground-breaking science across rare diseases such as Spinal Muscular Atrophy (“SMA”), brought to market the first CAR T cell therapy in a pediatric cancer indication, and pioneered the development of radioligand therapies for hard-to-treat cancers such as castration resistant metastatic prostate cancer. The commercial success of predecessor products made these incredible medical advancements possible, and that virtuous cycle continues to fuel the discovery of new medicines. In 2022 alone, Novartis had forty-four ongoing phase III programs and invested more than \$10 billion in research and development.²

OVERVIEW OF NOVARTIS COMMENTS

We recognize that CMS is required to implement the Negotiation Program on a timeline prescribed by statute. But, given the complexity of a program of this size and scope, with significant consequences across the multitude of stakeholders in the prescription drug supply chain, it is critical that CMS proceed carefully and deliberately in its approach to implementation to avoid further exacerbating the negative effects the law will have on future innovation and access to medicines in the U.S.

¹ CMS, Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (Mar. 15, 2023), available [here](#).

² Novartis, Novartis in Society: Integrated Report 2022 at 4 (Jan. 31, 2023), available [here](#).

Novartis' recommendations seek meaningful policy changes within CMS's authority under the statute to protect innovation, ensure patients have broad access to selected drugs, and construct robust safeguards to avoid diversion and facilitate access to the maximum fair price ("MFP") as required under the law. Novartis recognizes that, despite committing to "collaborating and engaging with the public" and "prioritiz[ing] transparency and robust engagement" in implementing the Negotiation Program,³ CMS finalized the fundamental policies set forth in Section 30 of the Initial Guidance, which govern the selection of drugs for negotiation for initial price applicability year ("IPAY") 2026, without providing any opportunity for public comment. Novartis objects to the agency's failure to allow for comment on Section 30, which would have allowed for public participation before the agency policies were finalized. Set forth below are comments that Novartis would have made had the agency provided an opportunity for comment on such policies, along with Novartis' comments on the sections in the Initial Guidance on which CMS is soliciting comment.

As detailed below, Novartis makes the following recommendations:

- Define a qualified single source drug by reference to its New Drug Application ("NDA") or Biologics License Application ("BLA");
- Protect orphan drug development within the framework of the statute;
- Replace the bona fide marketing standard with the Medicaid Drug Rebate Program ("MDRP") standard;
- Clarify that a selected drug should have preferred formulary placement;
- Set the MFP at the MFP ceiling where a small molecule drug is less than thirteen years post-approval or where the ceiling is based on the "plan specific enrollment weighted amount";
- Protect against the disclosure of confidential commercial information;
- Rescind the proposals to impose overly broad confidentiality obligations on manufacturers;
- Finalize the proposal to permit manufacturers to provide access to the MFP through a rebate model and ensure that manufacturers have the requisite information to do so;
- Ensure accurate use of 340B claims modifiers;
- Allow manufacturers to rely on reasonable assumptions with respect to information submission requirements;
- Consider only appropriate therapeutic alternatives as comparators; and
- Commit to further enabling real dialogue during the negotiation process.

As a member of Pharmaceutical Research and Manufacturers of America ("PhRMA") and the Biotechnology Innovation Organization ("BIO"), Novartis also supports their comments on the Initial Guidance.

SECTION 30 – IDENTIFICATION OF SELECTED DRUGS FOR IPAY 2026

- I. **CMS should rescind its policy governing the identification of a qualifying single source drug by reference to common active moiety (drugs) or common active ingredient (biologics), and instead identify such a drug by reference to its NDA or BLA, as required by statute.**

In the Initial Guidance, CMS states that it will identify a qualifying single source drug, and its dosage forms and strengths, by reference to common active moiety (drugs) or common active ingredient (biologics).⁴ **This policy will have devastating effects on innovation and patient access, and is irreconcilable with the statute, which dictates that a qualifying single source drug, and its dosage forms and strengths, be identified by reference to its NDA or BLA. CMS should therefore rescind this approach and instead adopt an application-based standard for distinguishing among qualifying single source drugs.**

Under section 1192, only "qualifying single source drugs" are eligible for selection for negotiation. Subject to certain exclusions, "qualifying single source drugs" are drugs or biologics for which there is no generic or biosimilar on the market and for which a statutorily prescribed time period has elapsed since approval or licensure.⁵ For drugs, "at least 7 years [must] have elapsed since the date of such approval" as of the selected drug publication date.⁶ And, for biologics, "at least 11 years [must] have elapsed since the date of such licensure" as of the selected drug publication date.⁷

³ Initial Guidance at 2.

⁴ *Id.* at 8.

⁵ Social Security Act ("SSA") § 1192(e)(1).

⁶ *Id.* § 1192(e)(1)(A)(ii).

⁷ *Id.* § 1192(e)(1)(B)(ii).

The statute clearly defines a “qualifying single source drug” by reference to a “covered Part D drug,” as that term is defined in the Medicare statute.⁸ The definition of a “covered Part D drug,” in turn, cross-references the definition of a “covered outpatient drug” in the MDRP statute.⁹ And, under such definition, whether a single source drug is a distinct “covered outpatient drug” is based on whether the product is approved pursuant to a distinct NDA or BLA.¹⁰ The only exception to this rule under the MDRP comes in the context of line extensions. There, Congress specifically amended the MDRP statute to enable line extensions to be grouped with innovator products across distinct NDAs or BLAs.¹¹ In contrast, Congress chose not to group drugs across distinct NDAs or BLAs under the Negotiation Program.¹²

In addition, the statutory definition of a “qualifying single source drug” also specifies that a qualifying product is subject to a statutory seven- or eleven- year clock tied to each “approval” or “licensure” of a product. It follows, then, that each qualifying single source drug corresponds to a distinct approval or licensure, *i.e.*, a distinct NDA or BLA. Any other reading—including one based on common active moiety or common active ingredient—contradicts the plain text of the statute.

Finally, the statutory “qualifying single source drug” definition is grounded in the Food and Drug Administration’s (“FDA’s”) framework for approving and licensing drugs and biologics, and such framework distinguishes among drugs and biologics via distinct applications.¹³ The FDA has spoken directly to the types of changes to an approved product that should be approved via a supplement to an existing NDA or BLA, and those that should be approved via a new NDA or BLA.¹⁴ By expressly cross-referencing the FDA framework in the “qualifying single source drug” definition, Congress clearly intended that CMS rely on such framework in distinguishing among qualifying single source drugs.

The use of NDAs and BLAs as the standard for distinguishing among qualifying single source drugs helps balance the twin interests in pharmaceutical and biotechnology innovation and lowering prescription drug prices. The statute seeks to ensure that the latter does not unduly outweigh the former by, among other things, establishing a period of time after approval or licensure during which a drug or biologic is not eligible for selection for negotiation, thereby preserving an incentive for manufacturers to research and develop next-generation products that will ultimately benefit patients. In contrast, CMS’s policy will greatly exacerbate the disincentive to develop next-generation therapies inherent in the Negotiation Program, to the detriment of patients in need.

II. CMS should act to protect orphan drug development.

The statute excludes from the definition of “qualifying single source drug” a drug that is “designated as [an orphan drug] for only one rare disease or condition . . . and for which the only approved indication (or indications) is for such disease or condition.”¹⁵ This orphan drug exclusion is aligned with Congress’s long-standing recognition of the profound governmental interest in facilitating the development of orphan drugs to meet needs that would otherwise go unmet, including through the Orphan Drug Act (“ODA”).¹⁶ The IRA provides that a drug loses its status as an excluded orphan drug where an orphan indication for a second rare disease or condition is approved; a non-orphan indication is approved; or the drug is designated as an orphan drug for a second rare disease or condition. Manufacturers commonly seek indication approvals and orphan designations sequentially as new clinical evidence is developed. Therefore, drugs qualifying for the orphan drug exclusion can lose eligibility for the exclusion with a subsequent indication and thereby become eligible for selection for negotiation.

Novartis appreciates CMS’s commitment in the Initial Guidance to “consider whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development.”¹⁷ CMS should clarify that, where a drug loses its status as an excluded orphan drug, the seven- or eleven-year selection clock starts on the date on which the drug loses such status. Without such a policy, the orphan drug exclusion would further disincentivize the development of multi-rare disease orphan drugs and cause companies to reprioritize their product pipelines accordingly. CMS should not needlessly erect additional barriers to the development of multi-rare disease orphan drugs. Even with the

⁸ *Id.* § 1192(e)(1).

⁹ *Id.* § 1860D-2(e)(1).

¹⁰ *Id.* §§ 1127(k)(2), (k)(7)(A)(iv).

¹¹ Patient Protection and Affordable Care Act of 2010, Pub. L. No. 111-148, § 1206 (Mar. 23, 2010) (codified at SSA § 1927(c)(2)(C)).

¹² Notably, Congress did do so as to another provision of the IRA: The Part D inflation rebate provision specifically directs CMS to establish an inflation rebate formula for line extensions consistent with the formula under the MDRP. SSA § 1192(e)(1).

¹³ FDA, Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees (Dec. 2004), available [here](#).

¹⁴ *Id.* at 3.

¹⁵ SSA § 1192(e)(3)(A).

¹⁶ ODA, Pub. L. No. 97-414, §§ 1, 2, 96 Stat. 2049, 2049-2051 (1983), as amended by Pub. L. 98-551, 98 Stat. 2815, 2817 (1984).

¹⁷ Initial Guidance at 11.

ODA, most people suffering from rare diseases and conditions do not have an FDA-approved treatment option.¹⁸ Designing and completing clinical trials that satisfy FDA standards for such small populations present unique challenges and thus require significant investment of resources in a drug that, by definition, will be furnished or dispensed to a small number of patients.¹⁹ We urge CMS to take steps to mitigate this particular disincentive for multi-rare disease orphan drug development by clarifying that the seven- or eleven-year selection clock starts on the date on which a drug loses its status as an excluded orphan drug.

III. CMS should replace its bona fide marketing standard for determining whether a generic or biosimilar product is on the market with the MDRP market date standard.

In the Initial Guidance, CMS specifies the standard by which a drug is rendered ineligible for selection for negotiation due to a generic or biosimilar product entering the market. CMS states that it intends to review prescription drug event (“PDE”) data to determine whether a generic or biosimilar satisfies a “bona fide marketing” standard, under which the agency makes a subjective judgment as to whether the degree of utilization of the generic or biosimilar represents “robust and meaningful competition.”²⁰ Novartis is deeply concerned with this approach, which lacks a logical nexus to the actual date of marketing and will introduce unnecessary complexities and confusion into the Negotiation Program. CMS should abandon the bona fide marketing standard and instead specify that both (1) the date on which an approved generic or biosimilar is marketed and (2) the date on which CMS determines that an approved generic or biosimilar has been marketed are the product’s “market date” for MDRP purposes.

As a definitional matter, marketing is “[t]he act[] . . . of bringing or sending a product or commodity to market.”²¹ As such, once the “action of buying or selling” has occurred, a product has necessarily been “marketed.”²² CMS itself has recognized that when a product is “marketed” is an objective point-in-time determination based on when the product enters the commercial marketplace for sale. For purposes of the IRA’s Part D inflation rebates, CMS proposed to determine when a product is “marketed” by reference to its “market date” as reported under the MDRP.²³ In turn, CMS’s longstanding policy under the MDRP has been to define “marketed” by reference to the date on which a product enters commercial distribution.²⁴ And, under the Part D program, which will source the PDE data on which CMS intends to rely in effectuating its bona fide marketing standard, CMS has recognized that the date on which a product is “release[d] onto the market” triggers certain coverage-related obligations²⁵—which means that CMS will have already recognized that a product has been released onto the market by the time PDE data show product utilization.

There is no basis for CMS to override the clear bright-line test imposed by the statute in favor of a subjective standard that effectively gives the agency unlimited discretion to determine whether and when a product is subject to an MFP. This is especially so given Congress has demonstrated that it knows how to establish a subjective “bona fide” standard yet declined to do so here.²⁶ “[W]here Congress knows how to say something but chooses not to, its silence is controlling.”²⁷

CMS’s unlawful bona fide marketing standard will also necessarily result in a delay between the actual date of marketing and the date of CMS’s determination because it takes time for sales to be reflected in PDE data. Indeed, as CMS permits Part D plan sponsors 180 days after a newly approved drug is released onto the market to determine whether to add the drug to their formulary, PDE data will rarely reflect when the drug came to market with accuracy. Many Part D plan sponsors will not add a newly approved drug to their formulary until the 180-day mark (or may not add it at all), and, thus, the first six months of PDE data following the market entry of the drug will necessarily reflect only very limited uptake.²⁸ Even where

¹⁸ FDA, Rare Diseases at FDA, available [here](#) (last accessed Feb. 27, 2023) (“Many rare conditions are life-threatening and most do not have treatments.”); National Organization for Rare Disorders, *New Study Investigates the Number of Available Orphan Products, Generics and Biosimilars*, Mar. 25, 2021, available [here](#) (reporting that *ninety percent* of rare diseases do not have an FDA-approved treatment).

¹⁹ See FDA, Guidance for Industry: Rare Diseases: Common Issues in Drug Development (Jan. 2019), at 1, available [here](#) (“Although the statutory requirements for marketing approval for drugs to treat rare and common diseases are the same . . . , these issues are frequently more difficult to address in the context of a rare disease for which there is often limited medical and scientific knowledge, natural history data, and drug development experience.”); B. Adams, *More Than a Quarter of Rare Disease Trials Are Culled Due to Low Patient Rates: Report*, Fierce Biotech, Mar. 11, 2021, available [here](#).

²⁰ Initial Guidance at 67.

²¹ Oxford English Dictionary, Definition of Marketing, available [here](#) (last accessed Mar. 26, 2023).

²² *Id.*

²³ CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, at 18 (Feb. 9, 2023), available [here](#); FDA, National Drug Code Directory (July 22, 2022), available [here](#). With respect to the IRA’s Part B inflation rebate, CMS proposed to determine when a product is “marketed” by reference to the “date of first sale” that the manufacturer must report for average sales price (“ASP”) purposes, which likewise is an objective point-in-time determination. CMS, Part B Inflation Rebate Guidance: Use of the 340B Modifiers, at 13-14 (Dec. 20, 2022), available [here](#).

²⁴ 83 Fed. Reg. 12,770, 12,784 (Mar. 23, 2018) (MDRP National Rebate Agreement); see also 42 C.F.R. § 447.502.

²⁵ CMS requires that Part D plan sponsor P&T committees “make a reasonable effort to review a new FDA approved drug product (or new FDA approved indication) within 90 days of its release onto the market and . . . make a decision on each new FDA approved drug product (or new FDA approved indication) within 180 days of its release onto the market, or a clinical justification will be provided if this timeframe is not met.” Prescription Drug Benefit Manual, ch. 6 § 30.1.5.

²⁶ SSA § 1927(k)(1)(B)(i)(II) (as amended by Pub. L. No. 111–148, § 2503(a) (2010)) (amending the MDRP statute to specify that only “bona fide” service fees are exempt from the calculation of average manufacturer price).

²⁷ *Animal Legal Def. Fund v. U.S. Dep’t of Agric.*, 789 F.3d 1206, 1217 (11th Cir. 2015).

²⁸ While plan enrollees may access a non-formulary drug via an exceptions process, access may not be immediate under such process; moreover, exception processes typically yield only a very small volume of utilization.

plan sponsors add the drug to their formulary, there is typically a gradual transition by providers and patients to such product as they become increasingly familiar with its benefits relative to alternatives.²⁹ Such a product is in fact **marketed** during this uptake period, but CMS's standard ignores this fact and focuses instead on whether the product is adequately **utilized**.³⁰ ***Such changes in utilization patterns over time do not mean that the market is not working as intended.***

CMS's standard is all the more concerning given the agency's intent to review PDE data only **once per month** for purposes of determining when the MFP terminates,³¹ which compounds the lag between the actual date of marketing and the date of CMS's determination.

It is especially critical that CMS equate the date of CMS's determination of marketing with the MDRP's "market date." If there is a lag of even one day between the date of CMS's determination and the actual date of marketing, the selected drug may be subject to the MFP for an additional twelve months. This risk would materially disincentive generic and biosimilar entry because a potential generic or biosimilar manufacturer would be concerned about its product's ability to compete with the selected drug's MFP for an unduly extended time. This outcome would run contrary to Congress's objective in promoting generic and biosimilar market competition under the Negotiation Program.

SECTION 40 – REQUIREMENTS FOR MANUFACTURERS OF SELECTED DRUGS FOR IPAY 2026

I. CMS should ensure robust safeguards are in place to protect against disclosure of confidentiality commercial information.

Novartis welcomes CMS's stated commitment to confidentiality in the Initial Guidance but asks CMS to establish more robust safeguards to protect a manufacturer's confidential commercial information from disclosure. Manufacturers will be required to submit a host of highly sensitive information to CMS, including research and development costs, production and distribution costs, and revenue and sales volume data.³² Novartis asks CMS to adopt the following measures to protect against the disclosure of confidential commercial information.

A. Scope of protection of confidential commercial information

The statute provides that whether information submitted by a manufacturer is proprietary is left to the discretion of the agency. In "implement[ing] a confidentiality policy that is consistent with existing requirements for protecting proprietary information,"³³ Novartis asks CMS to ensure protections comparable, not only to those under the Freedom of Information Act ("FOIA"), but also to those under other federal programs including Medicare, Medicaid, and the 340B Program.

B. Storage and access requirements

CMS should also commit to ensuring that all confidential commercial information, including information in the Health Plan Management System ("HPMS") and in electronic communications with the agency, will be stored in a secure manner, accessible only by those CMS staff who have a program-based reason to access the information. CMS has instituted similar measures with respect to product and pricing data submitted by manufacturers under the MDRP.³⁴

C. Confidentiality safeguards regarding the public explanation of the MFP

The statute requires CMS to publish an "explanation for the maximum fair price with respect to the factors as applied under section 1194(e) for such drug."³⁵ Without sufficient safeguards in place, Novartis is concerned with the potential for improper disclosure of confidential commercial information. Novartis welcomes CMS's commitment in the Initial Guidance to provide only high-level comments regarding manufacturer-submitted data and to refrain from disclosing proprietary information, but this alone is insufficient to protect against the inadvertent disclosure of confidential commercial information that is protected

²⁹ See A. Lubby, *Factors Affecting the Uptake of New Medicines: A Systematic Literature Review*, 14 BMC HEALTH SERVICES RESEARCH 469 (2014) (describing the various factors that affect early uptake of new medicines).

³⁰ Other examples of deficiencies in CMS's approach include circumstances where low utilization is driven by uncontrollable factors such as supply shortages.

³¹ Initial Guidance at 62.

³² SSA § 1194(e)(1).

³³ Initial Guidance at 29.

³⁴ CMS, *Medicaid Drug Programs ("MDP") User Manual* 1 (Nov. 3, 2021). In particular, data submitted by manufacturers under the MDRP are uploaded to an online interface that is used by states and manufacturers. States do not have access to quarterly or monthly pricing records or all product information because some of this information is confidential.

³⁵ SSA § 1195(a)(2).

under the statute.³⁶ CMS should commit to affording manufacturers a reasonable opportunity to review the intended explanation of the MFP in advance of publication.

II. CMS should rescind its proposals to impose overly broad confidentiality obligations on manufacturers.

CMS proposes to impose significant restrictions on what information a manufacturer may disclose and what records a manufacturer may keep regarding the negotiation process. These restrictions raise significant legal and policy concerns and betray the core principles animating our nation. Ensuring that the nation's public policy is fully informed, which is to the benefit of all, requires that manufacturers be enabled to speak freely about their direct experiences with the government's administration of its programs, especially one as consequential as the Negotiation Program. And such open exchange furthers the efficient administration of the Negotiation Program by ensuring that manufacturers can participate with the benefit of insight into past experiences of other manufacturers.

To start, CMS's chilling restrictions on manufacturer expression violate manufacturers' basic First Amendment "right to speak freely" and are therefore unconstitutional.³⁷ The Initial Guidance would compel manufacturer silence through the threat of civil monetary penalties ("CMPs") of \$1 million per day for as long as the negotiation agreement is in effect.³⁸ This prospect of effectively limitless CMPs raises grave concerns under the Eighth Amendment's prohibition against excessive fines.

Moreover, CMS's proposals cannot be reconciled with the obligations of manufacturers to their boards, shareholders, and other relevant constituents. Manufacturers have obligations to make material information available to shareholders and must maintain records to facilitate this obligation;³⁹ CMS's proposals could result in liability for manufacturers under federal and state securities laws. A manufacturer would be prohibited from using what it learns during the negotiation process to update its stated expectations. Such prohibition could expose the manufacturer to liability for failing to provide material information to investors. CMS's proposals are also inconsistent with securities law requirements to maintain appropriate disclosure controls and procedures, which are often predicated on record-keeping.

In addition, CMS's post-negotiation agreement termination record destruction proposal is unenforceable. The requirement imposes an extreme burden on manufacturers that far outweighs any purported benefit in keeping such information confidential post-termination. In particular, the destruction obligation would interfere with manufacturers' ability to comply with their record-keeping obligations and engage truthfully with their regulators, affiliates, contract parties, customers, and the market at large. CMS's record destruction proposal is also unlawful because it would prevent manufacturers from retaining records that they may need to protect against mistaken, yet significant, CMPs for noncompliance.⁴⁰ Requiring manufacturers to destroy such records raises fundamental concerns under the Due Process Clause of the Fifth Amendment.⁴¹

III. CMS should finalize its proposal to allow manufacturers to provide access to the MFP through a rebate model but ensure access to claims data that will allow manufacturers to appropriately verify MFP eligibility.

Novartis applauds CMS's proposal to permit manufacturers to provide access to the MFP through a rebate model, which is essential in safeguarding against diversion of MFP units. There are two ways that a rebate model could be effectively implemented: (1) a manufacturer-administered model; and (2) a CMS-established third-party administrator ("TPA")-administered model. ***CMS should enable manufacturers to effectuate MFP rebates through either model, at their election.***

For both the manufacturer-administered model and the TPA-administered model, it is critical that manufacturers have access to the claims data needed to appropriately verify MFP eligibility. Under the manufacturer-administered model, the provider or pharmacy would need to submit to the manufacturer the necessary Medicare claims data in order to qualify for the rebate. And, under the TPA-administered model, the TPA would need to have access to the necessary Medicare claims

³⁶ Initial Guidance at 29.

³⁷ *Wooley v. Maynard*, 430 U.S. 705, 714 (1977).

³⁸ Initial Guidance at 69.

³⁹ Almost all states require corporations to maintain records and permit shareholders to inspect their books and records. See, e.g., 8 Del. C. § 220 (describing the power of a shareholder to demand inspection of a corporation's books and records).

⁴⁰ Initial Guidance at 69–70.

⁴¹ Courts have recognized that "the essence of due process is fundamental fairness," and little could be more fundamentally unfair than requiring destruction of the very records that a manufacturer needs to verify its innocence against the imposition of an erroneous penalty. *Evans v. Wilkerson*, 605 F.2d 369, 371 (7th Cir. 1979).

data in order to validate claims and invoice MFP liability. The TPA would also need to serve as a Medicare claims data clearinghouse through which manufacturers can obtain all such data, including the 340B claims modifier information discussed below, in order to validate the propriety of the TPA-invoiced MFP rebate liability. Access to such data for claims validation is standard practice in the commercial marketplace today. CMS should ensure both MFP rebate models leverage such existing best practices to ensure that all necessary data are available to verify MFP eligibility and support the integrity of the Negotiation Program.

By statute, a pharmacy or provider may not purchase a unit of a selected drug at the MFP and then dispense or furnish it to an MFP-ineligible individual. Even though there is a clear prohibition against MFP diversion, neither manufacturers nor CMS has a statutory right to audit pharmacies and providers to validate proper dispensing and furnishing of MFP units. There is also no statutory means through which pharmacies and providers can be penalized for improperly dispensing or administering MFP units to MFP-ineligible individuals, such as by terminating the pharmacies' or provider's access to the MFP. Given the lack of a retrospective mechanism to protect against diversion of MFP units to MFP-ineligible individuals, the need for a rebate model to provide prospective protection against such diversion is imperative.

Additionally, a rebate model is easy to implement because stakeholders are well familiar with this model in the commercial sector and under the Part D program. And the MFP rebate model would not jeopardize Medicare beneficiary access to reduced MFP-based cost-sharing, as pharmacies and providers will know at the time a unit of a drug is dispensed or furnished that the drug is a selected drug and will be able to adjust cost-sharing accordingly.

However, to effectuate a functional rebate model, it is essential that CMS clarify that the proposed fourteen-day period during which a rebate must be paid runs from the date on which the manufacturer validates eligibility for the rebate.⁴² The Initial Guidance is silent on when the fourteen-day clock begins to run. If the clock were to run from the date on which the rebate is requested, the diversion safeguard provided by the proposed rebate model would be rendered meaningless. There would be no incentive for a provider or pharmacy to provide any validating Medicare claims data.

Finally, while Novartis applauds CMS's recognition of the need for a rebate model, we recognize that the precise details of how a rebate model would be operationalized will require further development through collaboration among all affected stakeholders. We urge CMS to support that collaboration by facilitating engagement across industry to help ensure that the rebate process works efficiently.

IV. CMS should ensure accurate use of 340B claims modifiers.

By statute, a manufacturer of a selected drug has no obligation to offer both the MFP and the 340B price on the same unit.⁴³ The manufacturer is obligated only to offer the lower of the two prices. It is therefore vital that CMS put in place a mechanism to prevent 340B-MFP duplicate discounts.

While CMS has already taken welcome steps to require the use of a 340B claims modifier for drugs reimbursed under Part B starting on January 1, 2024,⁴⁴ and is proposing to require the same for Part D drugs,⁴⁵ no comparable steps have been taken for Part B drugs reimbursed under Medicare Advantage ("MA") or to protect against 340B-MFP duplicate discounts. And, in the Initial Guidance, CMS includes no meaningful proposal as to how the prohibition on MFP-340B duplicate discounts will be effectuated.⁴⁶ To help ensure that 340B units can be identified, it is imperative that CMS require the use of either a 340B or a non-340B claims modifier on a claim for reimbursement for a selected drug, across Part B, MA, and Part D, and to make such requirement enforceable, by conditioning payment of such claim on the accurate use of such modifier.

The statutory prohibition against 340B-MFP duplicate discounts obligates CMS to establish a meaningful mechanism for identifying 340B units,⁴⁷ which is especially critical given the long and well-documented history of widespread 340B covered

⁴² Initial Guidance at 40.

⁴³ SSA § 1193(d).

⁴⁴ CMS, Part B Inflation Rebate Guidance: Use of the 340B Modifiers (Dec. 20, 2022), available [here](#).

⁴⁵ CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum 18 (Feb. 9, 2023), available [here](#).

⁴⁶ See Initial Guidance at 66.

⁴⁷ See *United States v. Markgraf*, 736 F.2d 1179, 1183 (7th Cir. 1984) ("An administrative agency cannot abdicate its responsibility to implement statutory standards under the guise of determining that inaction is the best method of implementation.").

entity non-compliance with the 340B-MDRP duplicate discount prohibition.⁴⁸ And, unlike 340B-MDRP duplicate discounts, there is no statutory audit, dispute resolution, or penalty process to remediate 340B-MFP duplicate discounts.⁴⁹ Given that the risk of 340B-MFP duplicate discounts is even higher than that of 340B-MDRP duplicate discounts, it is that much more vital that CMS establish a meaningful mechanism to protect against such duplicate discounts. We therefore strongly urge CMS to mandate that payment of a claim for reimbursement for a selected drug is conditioned on accurate use of either a 340B or a non-340B claims modifier, under Part B, MA, and Part D.

V. CMS should allow manufacturers to rely on reasonable assumptions with respect to information submission requirements.

As part of the negotiation process, manufacturers will be required to submit a wide range of information to CMS.⁵⁰ Because there may inevitably be ambiguities in how complex information submission requirements interface with equally complex business practices, and to ensure the process can be operationalized, CMS should clarify that manufacturers may rely on reasonable assumptions when interpreting statutory terms regarding the submission of data under the Negotiation Program. This is consistent with CMS's long-standing policy to allow manufacturers to use reasonable assumptions in the ASP and MDRP reporting contexts.⁵¹ CMS can and should adopt a similar framework here and enable manufacturers to make reasonable assumptions when submitting required information under the Negotiation Program. A framework permitting reasonable assumptions is far preferable to the rigid standardization that CMS proposes, and that the agency should abandon.⁵²

SECTION 60 – NEGOTIATION PROCESS

Novartis has serious concerns that the negotiation process as outlined in the Initial Guidance falls short of the level of transparency and engagement that would be appropriate given the significant consequences associated with the outcome of this process. CMS should adopt the following recommendations to enhance its proposed negotiation process.

I. CMS should consider only appropriate therapeutic alternatives as comparators.

Prior to the start of any negotiations, CMS should conduct a comprehensive review and publish guidance on the processes and criteria that will be used for selection of therapeutic alternatives. This review should include the relevant stakeholders, namely patient groups, health care professionals, clinical societies, and manufacturers. The establishment of the process and criteria for selection of appropriate therapeutic alternatives should allow time for public review and comment. The creation of robust criteria and process should be based solely on the scientific consensus around which products are truly therapeutically equivalent in both clinical effectiveness and patient treatment burden. This will help to ensure that patients' access to needed medications is driven by balanced clinical considerations and not based solely on cost differences between medications that are not truly equivalent.

Novartis encourages CMS to clarify that therapeutic alternatives to a selected drug would be those in the same drug class, have the same methods of action, and are approved for the same indications and patient population and consistent with nationally recognized, evidence-based guidelines. Additionally, they should have comparable efficacy and safety, and be administered through the same route of administration with similar dosing schedules. Finally, proposed therapeutic alternatives should have comparable real-world patient use to the comparator product. This would help increase the likelihood that the therapeutic alternatives that serve as comparators for purposes of the MFP negotiation are truly appropriate.

During the process of selecting specific therapeutic alternatives for individual drug negotiations, Novartis strongly encourages CMS to provide a fully transparent process on the criteria used to select therapeutic alternatives and the actual proposed alternatives and allow for public comment on those proposed alternatives. CMS should specifically seek input

⁴⁸ See, e.g., Government Accountability Office ("GAO"), Drug Discount Program: Federal Oversight of Compliance at 340B Contract Pharmacies Needs Improvement, GAO-18-480 (2018), available [here](#); see also 42 U.S.C. § 256b(a)(5)(A).

⁴⁹ Compare SSA § 1193(d) with Public Health Service Act § 340B(a)(5)(C), (d)(2)(v), (3).

⁵⁰ SSA § 1194(e)(1); see also *id.* §§ 1193(a)(4), 1194(b)(2)(A).

⁵¹ See, e.g., 71 Fed. Reg. 69,624, 69,667 (Dec. 1, 2006) (reasonable assumptions regarding ASP reporting); 83 Fed. Reg. at 12,785 (MDRP agreement provision governing reasonable assumptions).

⁵² See Initial Guidance at 82-91.

from patients currently on those medications, patient advocacy groups, health care providers, health care guidance committees, manufacturers, and other key stakeholders on the appropriateness of those comparators.

II. CMS should set the MFP at the MFP ceiling for small molecule drugs until at least thirteen years post-approval.

As noted at the outset of our letter, given the complexity and consequences associated with the Negotiation Program, Novartis strongly recommends specifying circumstances under which the MFP of a selected drug will be set at the MFP ceiling.

To be selected for negotiation, biologics (large molecules) must be at least eleven years post-licensure, while drugs (small molecules) must be at least seven years post-approval.⁵³ Because of the approximately two-year time lag between selection for negotiation and application of the MFP, an MFP cannot apply to a biologic until at least approximately thirteen years post-licensure and to a drug until at least approximately nine years post-approval. To help preserve small molecule innovation in parity with large molecule innovation, we urge CMS to specify that, for a small molecule drug, the MFP will not be set below the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.

We are concerned that the nine- and thirteen-year price applicability distinction arbitrarily promotes large molecule biologic innovation to the detriment of small molecule drug innovation. Studies have showed that most products (whether small or large molecules) achieve modest levels of annual sales in their first five years on the market.⁵⁴ Disincentivizing manufacturers from investing in small molecule drugs presents serious risk to patient access to effective treatment. And, while patients benefit from access to both types of products, small molecule drugs figure more prominently in the treatment plans of most Americans because they are more easily administered and utilized by patients.⁵⁵ For these reasons, we ask that CMS act to better balance the incentives regarding small molecule drug and biologic development by setting the MFP for a small molecule drug at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.

III. Where the MFP ceiling is based on the “plan specific enrollment weighted amount,” CMS should set the MFP at the ceiling price.

In designing the Part D program, Congress sought to establish a market-based system to provide Medicare beneficiaries with affordable drug coverage while maintaining robust access to diverse medicines needed to best manage their health conditions. Due to these market mechanisms, beneficiaries can now select from numerous plan options based on their premiums, formularies, and benefit designs. In addition, manufacturers of drugs with brand-brand competition negotiate substantial rebates to Part D plan sponsors, which enables greater patient access through improved formulary coverage and tier placement. These price concessions have grown over the years; the Medicare Payment Advisory Commission (“MedPAC”) noted that they reduced gross Part D expenditures by twenty-two percent in 2020.⁵⁶ As a share of brand expenditures, these rebates can reduce gross expenditures much more, particularly in highly competitive therapeutic areas.

Under the statute, the MFP ceiling for a Part D drug may not exceed the lesser of three distinct price points, one of which is the sum of each “plan specific enrollment weighted amount” for each Part D prescription drug plan (“PDP”) or MA prescription drug (“MA-PD”) plan.⁵⁷ When this price point is used to set the MFP ceiling, the MFP ceiling will reflect pre-existing price competition in the Part D marketplace, such that CMS should avoid disrupting such market competition by setting the MFP for such drug at the MFP ceiling. This would allow beneficiaries to share in the savings generated by competition in the Part D program while maintaining the underlying market signals to innovator companies.

IV. CMS should commit to further enabling real dialogue during the negotiation process.

⁵³ SSA § 1192(e)(1).

⁵⁴ QuintilesIMS Inst., *Lifetime Trends in Biopharmaceutical Innovation: Recent Evidence and Implications*, at 2 (Jan. 2017).

⁵⁵ T. Morrow & L. H. Felcone, *Defining the Difference: What Makes Biologics Unique*, 1 *Biotechnology Healthcare* 24 (2004).

⁵⁶ MedPAC, *Analysis of Part D Data on Drug Rebates and Discounts* (Sep. 30, 2022), available [here](#).

⁵⁷ SSA § 1194(c)(1).

CMS proposes that, as part of the negotiation process, it will invite the manufacturer to meet only where the agency rejects a counteroffer.⁵⁸ Novartis appreciates CMS's recognition of the importance of real dialogue, as opposed to a superficial paper process. Real dialogue between CMS and the manufacturer comports with Congress's intent in mandating a "negotiation" process for setting the MFP and would benefit both parties to the negotiation by promoting greater transparency and information sharing, and thus a fairer and better-informed negotiation process. That said, Novartis is concerned that CMS is arbitrarily restricting its engagement with the manufacturer by (1) limiting meetings to the period after a counteroffer is rejected and (2) permitting no more than three meetings.⁵⁹ There is no logical basis for imposing such restrictions on the negotiation process, as engagement between CMS and the manufacturer can equally inform an initial offer, potentially sparing the parties the need to consider a counteroffer. Moreover, the parties may agree that one or more additional meetings would be helpful and productive in setting the MFP. Therefore, CMS should modify its proposal to enable real dialogue between the parties **throughout** the negotiation process, and specify that, where the agency rejects a counteroffer, additional meetings may be held **without limit** where both parties agree that they would be helpful.

SECTION 110 – PART D FORMULARY INCLUSION OF SELECTED DRUGS

CMS should act to ensure broad access to selected drugs for Medicare Part D beneficiaries. While the statute requires Part D plans place selected drugs on formulary, CMS must take additional steps to ensure improved patient access for these drugs.⁶⁰ Without these steps, the Negotiation Program has potential to disrupt the competitive landscape in Part D and cause beneficiaries to face higher—not lower—barriers to accessing selected drugs in 2026.

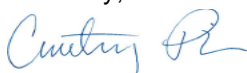
Stakeholders have long noted Part D plan preferences for products with higher prices and higher rebates; however, under the IRA, point-of-sale ("POS") prices for selected drugs in Part D will decrease to reflect the MFP plus any applicable dispensing fee. This decrease in POS prices for selected drugs may cause plans to prefer other drugs in their respective classes that are not selected, due to the potential for higher rebates. In response, plans may move selected drugs to tiers with higher cost-sharing or impose more restrictive utilization management in order to steer patients away from the selected drugs and toward alternatives that are able to provide more substantial rebates. This would run contrary to the intent of the Negotiation Program to ensure that Medicare beneficiaries will be able to access a selected drug at lower cost-sharing.

While formulary coverage is essential for providing beneficiaries access to selected drugs, CMS can and must go beyond the minimum requirements in the IRA. Specifically, we urge CMS to make clear that plans should not impose utilization management requirements, including prior authorizations and step therapy, that go beyond a selected drug's FDA-approved label. These requirements are clinically unnecessary, increase physician burden, and stand in the way of patients seeking to access selected drugs. Furthermore, we urge CMS to make clear that plans should place selected drugs on tiers requiring patient copayments rather than coinsurance. For selected drugs with monthly costs below the specialty tier cost threshold, this should be on the lowest generic tier on the plan's benefit design, while selected drugs with costs above this threshold could be placed on a higher copayment tier.

Taking these steps to improve patient access to selected drugs aligns with the intent of the Negotiation Program and stands to improve patient adherence to therapy. Furthermore, many of the drugs likely to be selected for IPAY 2026 treat chronic conditions where improved adherence is critical to improving patient outcomes and reducing non-drug costs under the Medicare program.

Novartis appreciates this opportunity to comment on the Initial Guidance and CMS's consideration of our feedback. We would be happy to discuss our comments at greater length. If you have any questions, please contact me by e-mail at courtney.piron@novartis.com.

Sincerely,



Courtney Piron
Head, US Public Affairs

⁵⁸ Initial Guidance at 55.

⁵⁹ *Id.* at 55-56.

⁶⁰ SSA § 1860D-4(b)(3)(I)



April 14, 2023

Submitted via Electronic Filing: IRAREbateandNegotiation@cms.hhs.gov

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RE: Novo Nordisk Comments on Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Dr. Seshamani,

Novo Nordisk Inc. (“Novo Nordisk”) appreciates the opportunity to provide comments in response to the memorandum issued by the Centers for Medicare & Medicaid Services (“CMS”), entitled *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments*.

Novo Nordisk is a global health care company committed to improving the lives of those living with serious chronic conditions, including diabetes, rare bleeding disorders, growth disorders, and obesity. The Novo Nordisk Foundation, our majority stakeholder, is among the top five largest charitable foundations in the world. Accordingly, our company’s mission and actions reflect the Foundation’s vision to contribute significantly to research and development that improves the lives of people and sustainability of society.

Novo Nordisk is a member of the Pharmaceutical Research and Manufacturers of America (“PhRMA”), and generally is aligned with PhRMA’s comments, and incorporates those comments herein, except in areas where our comments below diverge slightly.

As PhRMA’s comments and those in this letter demonstrate, CMS’s guidance lacks necessary detail and is inconsistent with the statute and Constitutional requirements that it, in its current form, cannot be finalized or used to implement the relevant provisions of the Inflation Reduction Act (“IRA”). Novo Nordisk believes that the guidance should be rescinded, and that CMS should start over in accordance with proper rulemaking that meets statutory and Constitutional requirements. However, reserving its rights to raise further objections as CMS continues to implement the IRA’s provisions, Novo Nordisk provides the following comments specific to certain aspects of the guidance and to assist CMS in properly implementing the IRA’s provisions.

CMS’S GUIDANCE UNLAWFULLY EXCEEDS THE SCOPE OF CMS’S DELEGATED AUTHORITY

Many of the provisions in CMS’s guidance exceed the scope of authority Congress granted to the agency and violate clear and specific statutory mandates. As the Supreme Court has recognized, when an agency takes actions that go “beyond what Congress has permitted it to do,” the agency has engaged in *ultra vires* conduct. *City of Arlington, Tx. v. FCC*, 569 U.S. 290, 299 (2013). An agency’s actions are *ultra vires* when it has exceeded the powers conferred upon it by law. See *Leedom v. Kyne*, 358 U.S. 184, 188 (1958); cf. *Compton v. Alpha Sorority, Inc.*, 64 F. Supp. 3d 1, 18 (D.D.C. 2014); *Central Transp. Co. v. Pullman’s Palace Car Co.*, 139 U.S. 24 (1891). An agency’s actions will also be struck down as *ultra vires* if they are “utterly unreasonable” or “contravene[] a clear and specific statutory mandate.” *Federal Express Corp. v. U.S. Dept. of Commerce*, 39 F.4th 756, 766 (D.C. Cir. 2022); see also *United States v. Cortez*, 930 F.3d 350, 357 (4th Cir. 2009) (noting that “any ‘improper[]’ agency action is ‘ultra vires’”).

Novo Nordisk is deeply concerned that CMS has not sought comment on certain parts of its guidance and, as described in more detail below, has not complied with basic notice-and-comment rulemaking requirements, even though the guidance seeks to impose substantive obligations on regulated parties that cannot be derived from the statute’s language. Deviating from proper procedures and deeming consequential parts of the guidance final with no opportunity for public comment is emblematic of a broader problem—CMS is using its guidance to rewrite the IRA. The IRA’s unprecedented price-control provisions present serious constitutional concerns on their own. Congress has not granted CMS free rein to rewrite statutory text and devise its own structure for imposing price controls on drugs and biologic products that Congress never intended.

Because CMS is unwilling to consider public feedback on certain sections of the guidance, including section 30, Novo Nordisk is not providing all of its comments on those parts of the guidance. Novo Nordisk instead reserves its rights to comment at an appropriate time and takes the position that any substantive obligations imposed by CMS that have not been promulgated through proper rulemaking procedures are invalid and cannot be enforced. Nonetheless, because many of the substantive requirements that CMS has deemed final have reverberating effects that extend throughout its guidance, including with respect to sections of the guidance for which CMS has solicited comment, Novo Nordisk will comment on certain aspects of the guidance that cut across its different sections. Indeed, many of the new requirements imposed by the guidance extend far beyond the scope of authority granted by Congress and violate specific statutory commands. A few examples are highlighted here:

First, CMS’s guidance purports to redefine “qualifying single source drug” (“QSSD”) in a way that contravenes the statutory definition prescribed by Congress. Congress granted no authority for CMS to rewrite the statutory definition or to expand the drugs potentially subject to price controls. Under the IRA, a “drug product” or “biological product” must satisfy several criteria to fall within Congress’s statutory definition of QSSD: (1) it must

be a “covered part D drug ... or a drug or biological product for which payment may be made under part B,” (2) it must be FDA approved (for drugs) or licensed (for biologics), (3) it must have been marketed pursuant to that approval or licensure for at least 7 years (for drugs) or 11 years (for biologics), and (4) it must not be the reference listed drug for an approved and marketed generic drug or the reference product for an approved and marketed biosimilar. *See* IRA § 1192(e). The IRA’s definition of QSSD does not expressly state or contemplate aggregating broad groupings of drug products as single QSSDs—and indeed, as detailed below, forecloses any such interpretation. Nor does it mention—anywhere in the IRA—the use of either active ingredient or active moiety as a defining characteristic.

CMS’s guidance effectively re-writes the statute and disregards the IRA’s unambiguous mandates by subjecting certain drugs to government-imposed price controls that the statute’s plain, unambiguous language made clear should not be subject to those controls. Redefining QSSD as an aggregation of products containing the same active moiety based on the date on which the *earliest* drug product with that active moiety (or the earliest biological product with that active ingredient) was approved, CMS’s guidance purports to sweep in innovative products that represent true advances for patient care that have not been marketed for the 7 or 11 years required by the statute. *See* IRA § 1192(e)(A)(ii) (defining QSSD as “[a] drug ... for which, as of the selected drug publication date with respect to such initial price applicability year, *at least 7 years will have elapsed since the date of such approval*) (emphasis added); *see also id.* at § 1192(e)(B)(ii) (defining QSSD as a “biological product” for which “as of the selected drug publication date with respect to such initial price applicability year, *at least 11 years will have elapsed since the date of such licensure*”) (emphasis added). In contravening the statutory definition of QSSD, CMS’s guidance improperly attempts to dramatically expand the number of drug and biologic products that are subject to price controls, eviscerating the incentives for continued innovation of previously approved active moieties and active ingredients ultimately to the detriment of patient health.

Second, CMS’s guidance seeks to override the IRA’s clear instructions on when a drug or biologic product no longer qualifies for price controls because a generic drug or biosimilar product has been marketed. *See* IRA § 1192(e)(1)(A); *id.* § 1192(c)(1), (2). Despite the statute’s plain terms specifying when a selected drug must be removed from negotiation, CMS’s guidance suggests that the agency intends to disregard the statute’s command unless and until CMS makes its own qualitative and subjective determination that there is “robust” and “meaningful” competition presented by the generic or biosimilar product. CMS’s guidance also suggests that it intends to expand its powers to determine when a competitor has engaged in “bona fide” marketing of a generic drug or biosimilar product.

The statute suggests that Congress did not intend to grant CMS such authority. To the contrary, Congress limited CMS’s authority by specifying which drugs qualify for negotiation. In particular, Congress was clear that (1) a drug will no longer be a QSSD once a generic drug or biosimilar is approved and marketed that relies on that drug as a reference listed drug (§ 1192(e)(1)(A)(iii)) or a reference product (§ 1192(e)(1)(B)(iii)), and (2) a negotiation-eligible drug will no longer be a selected drug for the initial price applicability year that begins

at least 9 months after a generic drug or biosimilar is approved and marketed (§ 1192(c)). In light of these plain statutory commands, the IRA does not grant CMS implicit authority to regulate competition between drug manufacturers.

The IRA also does not support the vague terms and arbitrary lines CMS seeks to draw by establishing metrics like “sufficient quantities” and “market share.” To the contrary, “commercial marketing” is a well-established and well-defined term: meaning the introduction or delivery for introduction into interstate commerce of a drug product. Indeed, in Appendix C of the guidance, CMS defines marketing plainly as “the introduction or delivery for introduction into interstate commerce of a drug product.”

“Marketing” is already defined in this way elsewhere in FDA and CMS regulations and guidance. *See, e.g.*, 21 C.F.R. § 314.3 (defining “commercial marketing” as “the introduction or delivery for introduction into interstate commerce of a drug product described in an ANDA, outside the control of the ANDA applicant”); 21 C.F.R. § 330.14(b)(2) (describing market history requirements for inclusion in the OTC drug monograph system); Medicaid Drug Rebate Data Guide for Labelers §4.15 (August 2018) (“Market Date: For S, I, and N drugs marketed under an FDA-approved application (e.g., BLA, NDA, ANDA), the earliest date the drug was first marketed under the application number by any labeler.”). Congress did not intend for CMS to adopt a new definition of “marketed” that is inconsistent with the definition previously and repeatedly established by HHS.

Third, CMS’s guidance impermissibly seeks to require the entity that holds an NDA/BLA for a selected drug (the “Primary Manufacturer”) to be responsible for collecting and submitting to CMS confidential and propriety information of *other* manufacturers, and enforcing pricing requirements on *other* manufacturers, including re-packers and re-labelers of the selected drug (“Secondary Manufacturers”). This new requirement presents significant Constitutional and practical concerns, and it also violates the statute. Nothing in the IRA distinguishes between “Primary Manufacturers” and “Secondary Manufacturers.” To the contrary, section 1191(c)(1) of the IRA states: “[t]he term ‘manufacturer’ has the meaning given that term in section 1847A(c)(6)(A) [of the SSA].” That definition cross-references section 1927(k)(5) of the Social Security Act, which also does not distinguish between primary and secondary manufacturers. *See* 42 U.S.C. § 1396r-8(k)(5). There is no indication that Congress intended to impose obligations on certain manufacturers—on threat of massive penalties—to be responsible for the submission of data and proprietary information of other manufacturers, especially given the enormous public policy and practical concerns that result from CMS’s approach. At a minimum, that extra-statutory obligation should not be imposed without complying with proper notice-and-comment rulemaking procedures.

CMS’s guidance ignores the enormous practical and/or legal problems that will result from CMS’s deviation from the statutory requirements. CMS’s guidance does not provide any mechanism for Primary Manufacturers to collect information from Secondary Manufacturers or to control the prices at which Secondary Manufacturers sell their goods. Thus, com-

pliance with such requirements cannot be ensured, placing manufacturers at risk of significant fines and penalties. Nor can CMS guarantee the confidentiality of the Secondary Manufacturers' proprietary information and data. Secondary Manufacturers who may be in contractual privity are still competitors (*e.g.*, authorized generic manufacturers) and ordinarily sharing this type of information risks violating the antitrust laws. CMS has previously recognized that forced sharing of data and information between competitors for price reporting purposes is not appropriate. *See* 81 Fed. Reg. 5267, 5266 (Feb. 1, 2016) ("We understand the [legal and logistical] challenges of obtaining pricing information from unrelated manufacturers. Therefore ... we have decided to limit the line extension provision to provide that a drug by one manufacturer will not be treated as a line extension of a drug by a different manufacturer, unless there is a corporate relationship between the manufacturers. This will limit the obligation of manufacturers to collect pricing information from unrelated parties."). The same consideration should apply here, especially because nothing in the statute supports CMS's proposed approach.

Fourth, CMS's guidance requires manufacturers to disclose significant confidential information that goes beyond the disclosures required by the statute. The manufacturer-specific data submission requirements outlined by section 50.1 and defined further in Appendix C greatly expand the scope of section 1194(e)(1) of the IRA by adding new data sub-elements and reporting requirements for each of the statute's requisite five data points. For example, CMS has broken the statutory requirement to report "research and development costs of the manufacturer for the [selected] drug and the extent to which the manufacturer has recouped research and development costs" into seven unique sub-elements (*e.g.*, "R&D: Basic Pre-Clinical Research Costs"), six of which include additional definitions, instructions, and de-facto sub-requirements. *See* Guidance Appendix C. In addition, CMS proposes to require that manufacturers report more than ten distinct product price points, six of which are not defined by the IRA, any other law, or otherwise required to be devised or reported by manufacturers (*e.g.*, "U.S. commercial average net unit price — without patient assistant program"). The guidance thus seeks to impose new substantive obligations on manufacturers without any explanation for these additional requirements and, contrary to the statute, fails to provide sufficient guarantees that the information provided by manufacturers will be held in strict confidence and protected from disclosure under all circumstances.

Fifth, CMS's guidance purports to institute a "gag" rule, precluding manufacturers from speaking truthfully about the "negotiation" process and the initial offers provided by CMS when setting the "maximum fair price" for a drug. CMS's guidance also proposes to require that manufacturers destroy negotiation information if the drug or biologic no longer qualifies as a selected drug. Nowhere in the IRA does Congress authorize CMS to impose these mandatory non-disclosure and information destruction provisions. These prior restraints on truthful speech are not contained in the statute. CMS has failed to provide any explanation why this proposal is necessary for purposes of administering the program.

CMS's guidance exacerbates First Amendment concerns already presented in the statute by silencing any dissent or even neutral information sharing about the "negotiation"

process. Indeed, because prior governmental restraints on speech “are the most serious and the least tolerable infringement on First Amendment rights,” *Nebraska Press Ass’n v. Stuart*, 427 U.S. 539, 559 (1976), they are subject to a “heavy presumption against [their] constitutional validity.” *Org. for a Better Austin v. Keefe*, 402 U.S. 415, 419 (1971) (quotation marks omitted). That principle applies with special force to restraints on the disclosure of “truthful information about a matter of public significance”—such as the data subject to use restrictions in section 40.2.2. Those types of restrictions are almost never permissible under the First Amendment. *Bartnicki v. Vopper*, 532 U.S. 514, 527 (2001).

**CMS’S GUIDANCE IS UNLAWFUL BECAUSE IT
DOES NOT COMPLY WITH ESSENTIAL
NOTICE-AND-COMMENT RULEMAKING REQUIREMENTS**

Even if the guidance were not in excess of CMS’s authority (which as outlined above, it clearly is), the guidance would be invalid because it seeks to impose substantive obligations on regulated parties and was not promulgated through proper notice-and-comment rulemaking procedures. The law is clear that an agency may not impose legal obligations on regulated parties through policy guidance. Guidance documents, like interpretive rules, are “not supposed to ‘have the force and effect of law’—or, otherwise said, to bind private parties.” *Kisor*, 139 S. Ct. at 2420 (quoting *Perez v. Mortgage Bankers Assn.*, 135 S. Ct. 1199, 1204 (2015) (internal quotation marks omitted)). They “are meant only to advise the public of how the agency understands, and is likely to apply, its binding statutes and legislative rules.” *Id.* (internal citation and quotation marks omitted).

In contrast, when an agency imposes substantive obligations that go beyond a statute’s express requirements, the agency must employ quasi-legislative rulemaking procedures with an opportunity for public notice and comment. *See Hoctor v. U.S. Dep’t of Agric.*, 82 F.3d 165, 170-71 (7th Cir. 1996); *see also Catholic Health Initiatives v. Sebelius*, 617 F.3d 490, 495 (D.C. Cir. 2010). These procedural requirements—as reflected in both the Administrative Procedure Act, *see* 5 U.S.C. § 553 *et seq.*, and the Social Security Act, *see* 42 U.S.C. § 1395hh(a)(2)—are essential to securing “the values of government transparency and public participation,” *Iowa League of Cities v. EPA*, 711 F.3d 844, 873 (8th Cir. 2013), by ensuring that agencies provide reasoned explanations for their decisions after evaluating and responding to comments. *See Azar v. Allina Health Servs.*, 139 S. Ct. 1804, 1816 (2019). They are also an essential part of a compromise that has allowed executive agencies to wield legislative rulemaking powers while accounting for the significant separation-of-powers concerns that arise from delegating such authority to executive agencies.

Congress has directed CMS to implement the statute’s requirements through guidance. *See* IRA § 1198(c). But that does not mean that CMS may read the word “guidance” to be a blank check that allows it to avoid all proper rulemaking procedures when it seeks to impose additional binding obligations on regulated parties. Nor is there good cause to waive essential notice-and-comment rulemaking requirements. The exceptions to rulemaking procedures are “narrowly construed and reluctantly countenanced.” *Mack Trucks*,

Inc. v. EPA, 682 F.3d 87, 93 (D.C. Cir. 2012). As a result, good cause for dispensing with rulemaking requirements never exists absent a showing of an emergency with the risk of “real harm.” *NRDC v. Evans*, 316 F.3d 904, 911 (9th Cir. 2003). That is especially true where, as here, Congress has not imposed “mandatory” deadlines, because it has not specified any consequences for CMS’s failure to comply with the suggested statutory deadlines. *Gottlieb v. Pena*, 41 F.3d 730, 734 (D.C. Cir. 1994). The statute does not provide for any sanction against CMS or HHS were the government to miss IRA implementation deadlines. Because there are no consequences specified in the statute, CMS is free to impose its own deadlines without any risk of a “coercive sanction” being imposed by the courts. *United States v. James Daniel Good Real Prop.*, 510 U.S. 43, 63 (1993). There is accordingly no reason CMS should not take the time needed to undertake proper rulemaking proceedings, including allowing public comment and responding to those comments before promulgating a final rule that is properly subject to judicial review.

**CMS’S GUIDANCE IS UNLAWFUL BECAUSE IT DOES NOT ADEQUATELY
PROTECT CONFIDENTIAL DATA AND PROPRIETARY INFORMATION,
AND IT UNDERMINES CONGRESSIONALLY-MANDATED INCENTIVES**

CMS’s guidance improperly lacks adequate safeguards to protect manufacturers’ confidential trade secret and other proprietary information. The guidance’s provisions call for the submission of confidential and trade secret information beyond what the IRA authorizes. While CMS’s guidance states that it will treat all such information as confidential, *see* Guidance § 40.2.1, there are multiple ways in which the data will not or cannot be held in confidence under the guidance.

Any unauthorized and unwarranted use or disclosure of a manufacturer’s proprietary information would be directly contrary to the IRA’s terms and would constitute an uncompensated taking of the manufacturer’s intellectual property. *See Ruckelshaus v. Monsanto*, 467 U.S. 986, 1001-04 (1984); *see also Philip Morris, Inc. v. Reilly*, 312 F.3d 24, 26 (1st Cir. 2002) (en banc) (holding that Massachusetts law allowing public disclosure of tobacco product ingredients resulted in an unconstitutional taking). It would also conflict with the government’s World Trade Organization trade secret and proprietary information obligations under the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) and FDA’s prohibition on disclosure of commercial confidential and trade secret information, *see* 21 U.S.C. § 331(j), 21 C.F.R. §§ 20.61, 314.430. Those provisions make clear that manufacturers have important property interests in their proprietary information, and those private rights must be protected and cannot be arbitrarily taken away by the government for its own benefit. In addition, any public disclosure of proprietary information would create serious antitrust and anticompetitive concerns that CMS should avoid.

More broadly, CMS’s guidance undermines statutory incentives for ongoing innovation of drugs and biologics. For example, CMS says that it will consider each broadly defined “drug” or “biologic” to be marketed based on the “earliest” approval of that active moiety or active ingredient. But by considering each active moiety (or active ingredient) to

be a QSSD, CMS captures for negotiation products that are still protected by regulatory exclusivity, regardless of whether the drug or biological product has been marketed for the requisite 7 or 11 years. This approach undermines the careful balance between innovation and competition that Congress has struck in the FDCA and PHSA, which carefully assigns market exclusivity based on *both* entry of a new active ingredient *and* continuing research and development into the potential of that active ingredient after approval. As a result, drug developers typically innovate in phases. Advancement in science is dependent on additional research for an initially developed product. Maintaining the economic value of incentives that result from incremental innovation by studying a molecule's mechanism of action, modified formulations of a previously approved product, and other product enhancements are critical to provide advancement in treatment and increased patient convenience (*e.g.*, oral vs injection, heat stable vs cold-chain supply, daily vs monthly treatment). This is precisely why Congress chose to incentivize incremental research under the FDCA and PHSA. But as described in more detail below, the statutory provisions designed by Congress, and overseen by FDA, to provide market exclusivity to certain products are wholly incompatible with CMS's rewrite of the IRA. *See* 42 U.S.C. § 262(k)(7) (reference product exclusivity); 21 U.S.C. § 355(c)(3)(E)(ii) and 21 U.S.C. § 355(j)(5)(F)(ii) (NCE exclusivity); 21 U.S.C. § 360cc(a) (orphan drug exclusivity); 21 U.S.C. § 355(c)(3)(E)(iii)-(iv) and 21 U.S.C. § 355(j)(5)(F)(iii)-(iv) (3-year exclusivity); 21 U.S.C. § 355a(b)(1)(A)(i)(I), 21 U.S.C. § 355a(c)(1)(A)(i)(I), 21 U.S.C. § 355a(b)(1)(A)(i)(II), 21 U.S.C. § 355a(b)(1)(A)(ii), 21 U.S.C. § 355a(b)(1)(A)(i)(II), 21 U.S.C. § 355a(c)(1)(A)(ii), 42 U.S.C. § 262(m)(2)(A), 42 U.S.C. § 262(m)(2)(B), 42 U.S.C. § 262(m)(3)(A), and 42 U.S.C. § 262(m)(3)(B) (pediatric exclusivity); 21 U.S.C. § 355f(a) (GAIN exclusivity).

CMS MUST RECOGNIZE AND ACCOMMODATE THE COMPLEXITIES ASSOCIATED WITH MANUFACTURER-SPECIFIC DATA SUBMISSIONS

Through section 50.1 and Appendix C of its guidance, CMS seeks to expand the five manufacturer-specific data elements enumerated in section 1194(e)(1) of the IRA into ten pages of additional definitions, imposing a slew of extra data gathering and submission requirements on manufacturers, many of which manufacturers have never devised, determined, calculated, or produced. CMS also envisions that Primary Manufacturers would have only 30 days to produce this information from not only their own records but also to collect and report much of this same information from Secondary Manufacturers. *See* Guidance § 50.1. The guidance notes that these requirements must be fulfilled within the specified timeframe to avoid a steep civil monetary penalty of \$1,000,000 per day of violation. *See id.* § 100.2. CMS will also require manufacturers to submit certifications regarding the completeness and accuracy of their data submissions.

Novo Nordisk is concerned that the manufacturer-specific data elements set forth in Appendix C of the guidance (1) would in part impose new substantive requirements on manufacturers that exceed the scope of the authority granted by Congress (among other problems, CMS requests pricing metrics that are not set forth in the IRA and that have never before been

established or devised); (2) cannot be implemented without notice-and-comment rulemaking because the IRA itself does not possess the requisite level of clarity to facilitate implementation of the manufacturer-specific data requirements through non-binding guidance; (3) would be misused by CMS for its own procurement purposes as a market participant and not for any regulatory reasons; and (4) would not be sufficiently protected from unauthorized use or disclosure beyond the negotiation program (CMS provides no details regarding its plans to protect this highly sensitive, proprietary information from unauthorized use or disclosure).

Besides being unlawful, the expansive requirements set out in Appendix C would pose a significant logistical challenge for manufacturers. Much of the information requested is not maintained in the ordinary course of business. The sheer quantity of the information that CMS proposes to extract from manufacturers may be both impractical and unfeasible within the short timeframe that CMS expects. For many companies, especially larger companies with complex operations, compiling this information would necessitate a coordinated and highly time- and resource-intensive approach. These efforts will be even more complicated for global companies like Novo Nordisk with headquarters that are based outside the United States, where information underlying many of the required data elements is spread across multiple individuals in various locations throughout the world. U.S. stakeholders would need to connect with global colleagues and other affiliates to access necessary information. These concerns would be further exacerbated if Primary Manufacturers would need to compile their own information while also coordinating data-gathering and reporting with Secondary Manufacturers, who may not be cooperative or responsive (and who will have significant concerns about providing their proprietary data to Primary Manufacturers, who often will be their competitors).

CMS should recognize that ensuring such a data set is complete and accurate will require considerable effort and time by manufacturers, greatly surpassing a limited period of 30 days. These complications will be particularly acute during the first year of negotiations for price applicability year 2026, when CMS will publish its list of 10 selected drugs on September 1, 2023 and expect Primary Manufacturers to submit the detailed data set out in Appendix C by October 2, 2023. Both manufacturers and CMS are sure to encounter complications and complexities that cannot be reasonably anticipated or accounted for until the process unfolds. Accordingly, Novo Nordisk has significant concerns that manufacturers will be able to provide the detailed data set out in Appendix C within just 30 days, especially for purposes of negotiations for initial price applicability year 2026.

Novo Nordisk believes that CMS has flexibility to implement the data submission timelines with respect to the manufacturer-specific data elements enumerated in section 1194(e)(1). CMS should afford manufacturers necessary and adequate time to prepare and submit data regarding the section 1194(e)(1) factors, and not implement a strict 30-day submission requirement envisioned by the guidance. The Agency should permit manufacturers to make rolling data submissions with respect to the section 1194(e)(1) factors, based on timelines that would be agreed to by CMS and each affected manufacturer. Such an approach would recognize the reality that there will be unavoidable circumstances in which more time is necessary to appropriately compile and provide accurate and complete data to the Agency. Moreover, CMS must

recognize and appreciate that manufacturers will need to make and rely on reasonable assumptions in providing much of the data to the Agency. The need to determine and rely on assumptions will be greater in the absence of informed and detailed guidance from CMS that meaningfully addresses the decisions and related complications that manufacturers will face in compiling and providing this data. (This issue also underscores the need for CMS to pursue notice-and-comment rulemaking.) Accordingly, CMS must afford manufacturers reasonable discretion to make assumptions in preparing their data submissions and cannot impose civil monetary penalties in relation to data submissions that are based on reasonable assumptions, especially if the Agency does not provide clear and detailed guidance that would directly conflict with a manufacturer's reasonable assumption.

**CMS'S GUIDANCE DOES NOT CONTAIN SAFEGUARDS
NECESSARY TO ENSURE THAT THE "MAXIMUM FAIR PRICE"
IS PROVIDED ONLY TO ELIGIBLE INDIVIDUALS**

Novo Nordisk respectfully suggests that the only way to operationalize access to the MFP consistent with the statute's terms is by providing a rebate to the dispensing entity, after validation of MFP-eligibility by a third-party administrator ("TPA"). For this process to work, the manufacturer and TPA will need sufficient claims-level data (please see Exhibit A of PhRMA's comment letter) and longer than the 14 days proposed by CMS. *See* Guidance at §40.4.

The nation's dispensaries are not equipped to maintain duplicative segregated inventories of MFP-priced selected drugs and non-MFP-priced selected drugs to serve the MFP-eligible and MFP-ineligible customers (respectively) who walk through their doors. Even a virtually segregated inventory will likely be too complex and onerous for this purpose. That is why dispensaries, which generally purchase at a common list price, effectuate the various discounts afforded to customers (via their insurance plans) not by purchasing at various discounts, but through after-the-fact rebates. The chargeback solution proposed by CMS in section 90.2 is not workable or appropriate. Chargebacks, based on saleable packages, support discounts when dispensaries are able to purchase from a wholesaler at a single point-of-purchase discount for all patients. Chargebacks are not an appropriate mechanism for extending discounts at the individual patient level.

Dispensaries should therefore access MFP by rebate, payable by the manufacturer on verified utilization by MFP-eligible individuals. The verification of MFP-eligibility is the key. Absent strong procedures to ensure that access to MFP be limited only to those individuals entitled to the price—consistent with the clear statutory language limiting MFP eligibility to individuals "enrolled in a prescription drug plan under part D ... or Medicare Advantage-prescription drug plan under part C"—the program risks operational failure and substantial abuse. Novo Nordisk urges CMS to be clear to participating dispensaries that diversion will not be tolerated.

CMS should require dispensaries to submit to a neutral TPA rebate claims with data sufficient to establish the MFP-eligibility of the patient to whom the selected drug was dispensed. The RxBIN and RxPCN data suggested by CMS at section 90.2 of the guidance are necessary but insufficient elements to achieve this purpose. Use of a TPA would standardize this process across manufacturers, which would eliminate the need for manufacturers to submit individual processes in writing to CMS. However, should CMS finalize its proposed approach, CMS should confirm that each manufacturer of a selected drug may make clear in its written process before the price applicability year what data elements are to be required to substantiate a claim for the MFP, such data elements not to be unduly onerous or inconsistent with standard business practices. Regarding a manufacturer's written process (if ultimately required), NNI urges CMS to treat such written process as proprietary and confidential, particularly as it could amount to disclosure of trade secret information. CMS should not publicize manufacturer processes.

Novo Nordisk agrees that dispensaries should be reimbursed timely when they are entitled to MFP rebates. The 14-day interval recommended in the guidance, however, is so tight as to be operationally infeasible. The IRA does not dictate a 14-day rebate mechanism, and CMS should not adopt one. In other government programs requiring eligibility verification and rebating, the timetable for rebates is more than twice as long (38 days in the Medicaid Drug Rebate Program and 38 days in the Part D Coverage Gap Discount Program). Novo Nordisk suggests that CMS require that dispensaries report their minimally necessary data sets to a TPA within a reasonable timeframe after the date of dispense, and that the manufacturer must pay the rebate (or issue a credit) to the dispensary within thirty-eight days of receipt of the complete MFP and 340B validation data from the TPA. Disputed or incomplete claims could be held pending resolution or completion.

Furthermore, the statute is clear that manufacturers may not be subjected to both the MFP and the 340B discount on the same unit. §1193(d). Rather, manufacturers of selected drugs must provide the lower net price to eligible patients. Many factors complicate application of this nonduplication requirement:

- 340B-covered entities purchase at both (a) the 340B price for 340B-eligible patients and (b) a non-340B price for ineligible patients (*e.g.*, Medicaid carve-out).
- Covered entities (and their TPAs) choose to identify eligible 340B patients well after a dispense to such patient has occurred, including sometimes many months after a dispense has occurred.
- There are no consistent, minimum standards or documentation requirements currently being enforced to ensure appropriate, transparent 340B patient identification.
- 340B-covered entities often utilize commercial contract pharmacies, outsourced dispensaries to patients of the covered entity made whole via replenishment.

- Covered entities and commercial contract pharmacies resist providing transparency and data to confirm 340B patient eligibility.
- Only some 340B pharmacy fills are to 340B-eligible patients, only some 340B fills are to MFP-eligible patients, and those populations only sometimes overlap.

Development of a mechanism that will address these varied complexities will be difficult, unless a TPA is used. It will therefore be necessary for CMS to coordinate with the Health Resources and Services Administration (“HRSA”) to ensure that manufacturers are subject to neither duplication of discounts nor diversion to ineligible patients.

In addition to these MFP-related concerns, a much larger issue exists with regard to 340B patient eligibility when drugs are dispensed through contract pharmacies. Manufacturers do not have adequate insight into which prescriptions are designated as 340B-eligible by a covered entity and why. Covered entity software vendors review contract pharmacy dispensing data in an effort to identify prescriptions associated with “patients of the covered entity;” however, this is defined at each covered entity. These software programs can even make strategic financial decisions and choose not to designate prescriptions as 340B-eligible if they are not sufficiently profitable. In many instances, multiple covered entities will claim 340B eligibility for the same prescription, leaving the manufacturer to pay a 340B chargeback multiple times for the same dispensed unit. These 340B program deficiencies, left unaddressed, will hinder the proper administration of the MFP.

CMS’s MFP guidance suggests that it may not yet be fully aware of the complexities of, or potential for ambiguity associated with, covered entities identifying 340B-eligible patients. Failure to appreciate and address these complexities could result in covered entities receiving both the MFP and a 340B discount for the same patient in violation of the IRA’s express requirements. CMS coordination with HRSA should focus on key areas that reduce the risk of duplicative discounts, including: (1) requiring that the identification of 340B-eligible patients and MFP-eligible patients must occur and be documented at the time of dispense; (2) establishing clear minimum documentation requirements for covered entities to support the identification of a 340B-eligible patient; and (3) for drugs subject to an MFP, requiring 340B discounts be paid as a rebate (as is currently the case with ADAPs) conditioned on the provision of adequate data to allow manufacturers to confirm the appropriateness of the discount and avoid duplicative MFP and 340B discounts.

**CMS SHOULD CLARIFY THAT PART D PLANS
MAY NOT IMPOSE PRIOR AUTHORIZATION OR STEP THERAPY
REQUIREMENTS FOR SELECTED DRUGS**

Novo Nordisk appreciates CMS's acknowledgement in the guidance that "[i]n accordance with section 1860D-4(b)(3)(I) of the Act, Medicare Part D plans shall include each covered Part D drug that is a selected drug on Part D formularies during [CY] 2026 and all subsequent years for which the MFP of the selected drug is in effect during the price applicability period." Guidance §110.

We urge CMS to specify that Part D plans may not impose utilization management requirements, such as prior authorization and step therapy, which effectively can result in non-coverage of a selected drug for a Part D beneficiary. That a product is "on formulary" does not mean beneficiaries will be able to obtain coverage for that therapy. As described further below, Medicare Part D plans are increasingly subjecting products on their formularies to prior authorization or step therapy requirements. Such restrictions violate the IRA when they are imposed on selected drugs.

Section 11001(b)(1)(E) of the IRA, which provides that "the PDP sponsor offering a prescription drug plan shall include each covered part D drug that is a selected drug..." is titled "Coverage of Selected Drugs." This language makes clear that Congress intended for selected drugs to be included on formulary such that they are actually covered for Part D beneficiaries. See *INS v. National Center for Immigrants' Rights*, 502 U.S. 183, 189-90 (1991) (citing *Mead Corp. v. Tilley*, 490 U.S. 714, 723 (1989) ("[T]he title of a statute or section can aid in resolving an ambiguity in the legislation's text....[Here] [t]he text's generic reference to 'employment' should be read as a reference to the 'unauthorized employment' identified in the paragraph's title.")). The statutory scheme further reinforces this direction from Congress. Specifically, section 1860D-2(d)(1)(D) of the Social Security Act, as amended by section 11001(b) of the IRA, provides that the benefits of the MFP for a selected drug must flow through to Part D beneficiaries by reducing the negotiated prices used in payment by each Part D plan sponsor for each selected Part D drug (which in turn form the basis for determining beneficiary cost-sharing). Guidance §40.4. Legislative history further describes that purpose of these provisions as "lowering costs for seniors and the Federal Government." H.R. Rep. No. 117-130, at 5 (2021). Medicare Part D beneficiaries (and the government) cannot realize the cost savings from the MFP for a selected drug if they are not able to obtain coverage for that selected drug.

Prior authorization and step therapy can result in non-coverage, even if a drug is included on a Part D plan formulary. Prior authorization requirements permit coverage denials for failure to seek and obtain prior authorization and step therapy mandates that a beneficiary try and fail on a different therapy before the Part D plan will cover the patient's prescribed

therapy. Both of these restrictions can deny coverage for prescribed therapies, potentially making them unavailable when a patient needs them, and place extra burdens on providers that discourage them from prescribing and dispensing these medically necessary medicines to patients. CMS has previously recognized that prior authorization and step therapy requirements can have the same effect on patients as non-coverage. In the context of Part D transition coverage, the Medicare Part D manual explains:

CMS defines non-formulary Part D drugs to mean: (1) Part D drugs that are not on a sponsor's formulary, (2) drugs previously approved for coverage under an exception once the exception expires, and (3) Part D drugs that are on a sponsor's formulary but require prior authorization or step therapy, or that have an approved QL lower than the beneficiary's current dose, under a plan's utilization management requirements. *This is because a formulary drug whose access is restricted via UM requirements is essentially equivalent to a non-formulary Part D drug to the extent that the relevant UM requirements are not met for a particular enrollee.*

Medicare Prescription Drug Benefit Manual, Chapter 6, § 30.41 (emphasis added).

CMS has also previously recognized that these types of utilization management impose barriers to patients' access to the particular treatment prescribed to them, which could adversely affect the progression of a patient's disease and their overall health. For example, in its 2018 proposed rule regarding the Part D protected classes, CMS cited a number of studies that suggested step therapy may be costly, both economically and with regard to patient health. *See* 83 Fed. Reg. 62152, 62187 (Nov. 30, 2018). CMS acknowledged that "[s]everal studies show that enrollees become discouraged when step therapy is used" and that the delay caused by step therapy "may cause a worsening of conditions leading to increased medical costs." *Id.* Such a result is not only harmful to beneficiaries, but it runs counter to Congress's goals in enacting the IRA: to help patients afford the medicines they need.

Accordingly, CMS should clarify in its revised guidance that Part D plans must provide coverage for selected drugs by including them on formulary without prior authorization or step therapy restrictions.

ADDITIONAL COMMENTS

1. Appropriate Therapeutic Alternatives

The guidance states that to "identify potential therapeutic alternatives...of a selected drug, CMS intends to use data submitted by the Primary Manufacturer and the public, FDA-approved indications, indications included in CMS-approved Part D compendia, widely accepted clinical guidelines, and peer-reviewed studies." Guidance §60.3.1. Further, CMS "intends to begin by identifying therapeutic alternatives within the same drug class as the selected drug based on properties such as chemical class, therapeutic class, or mechanism of action before considering therapeutic alternatives in other drug classes." *Id.*

Identification of therapeutic alternatives must be guided by widely accepted clinical guidelines. Widely accepted clinical guidelines should be the authoritative sources for identifying therapeutic alternatives, superior to other sources of information. Failing to do so would be to the detriment to the lives and well-being of Medicare beneficiaries and would challenge broadly-established scientific consensus.

Clinical guidelines are developed by committees of experts who have analyzed the totality of the evidence, assessed and graded its quality according to accepted standards, and come to well-accepted and scientifically-grounded treatment recommendations. Such guidelines are unbiased, unsponsored, and driven by an analysis of clinical benefit conducted by practitioners who have experience treating patients with specific conditions. CMS has acknowledged the importance of well-respected organizations that develop clinical practice guidelines. For example, the American Diabetes Association (ADA) is one of two organizations with accreditation power within its Diabetic Self-Management Training Accreditation Program.

Additionally, in multiple instances within the guidance, CMS notes its intention to prioritize the consideration of evidence relevant to Medicare populations, including adults over age 65, patients with end-stage renal disease, and disabled persons. To fully accomplish this, CMS must take into consideration the differing clinically-appropriate therapeutic alternatives for relevant subpopulations with large presence in Medicare such as multi-morbid Type 2 diabetes patients who may be living with chronic kidney disease (CKD) or those with atherosclerotic cardiovascular disease ASCVD. For example, while the American Diabetes Association (ADA) guidelines are the lodestar for diabetes patients broadly, there are separate clinical guidelines developed by Kidney Disease – Improving Global Outcomes (KDIGO) that risk stratify diabetes patients with chronic kidney disease which specify different treatment options for patients at various stages of the disease.

2. 30-Day Equivalent Supply

CMS proposes to calculate the MFP across dosage forms and strengths based on a “30-day equivalent supply.” Guidance §60.1. This approach is not feasible for medications such as insulin, as dosing is based on numerous factors not readily reduced to a common 30-day supply. For example, patients with Type 1 diabetes will use a larger amount of insulin in a 30-day timeframe than will patients with Type 2 diabetes. Patients who have diabetes and are living with obesity will have a higher starting dose per day than people with diabetes who have an “average” BMI. Type 2 patients can also become insulin resistant as they progress along their disease state and may require more dosing than a patient earlier in their disease state. Finally, patients will titrate their dosage differently based on their A1c values. CMS should re-evaluate their proposal to use a standard 30-day supply for applying the MFP across dosage forms and strengths to account for the wide variation in dosing for medications like insulin.

3. Use of FSS Price as MFP Reference

Novo Nordisk objects to the use of the Federal Supply Schedule (FSS) or Big 4 price as a reference point for the initial offer. Guidance §60.3.2. The FSS/Big 4 price contains negotiated discounts offered specifically to the Veterans Administration and the Department of Defense; discounts that are generally not available commercially. Reference to FSS and Big 4 prices could have the unintended consequence of reducing or eliminating voluntary manufacturer discounts that lead to lower prices for those government channels. CMS will remember a similar situation that occurred after the creation of Best Price in the MDRP in 1990. By failing to exclude prices to these government purchasers from Best Price, many of the voluntary discounts were withdrawn. See N. Fisher, *The 340B Program: A Federal Program in Desperate Need of Revision After Two-And-A-Half Decades of Uncertainty*, 22 J. Health Care L. & Policy 25 (2019). CMS should preserve the ability of the VA to negotiate deep discounts by removing the FSS price from the set of prices considered when developing an initial offer.

* * * *

The IRA's unprecedented drug pricing provisions raise serious constitutional and rule-of-law concerns. If prices for medications are not set at appropriate levels, the resulting market distortions could undermine innovation, discourage research and development, deprive patients of life-saving medications, and undermine the nation's healthcare system. In these circumstances, it is imperative that CMS comply with constitutional requirements and remain within the bounds of its proper authority. It must ensure that it follows rulemaking procedures, provides notice and opportunities for public comment, and responds meaningfully to objections. And it must respect and protect manufacturers' private rights. Instead of complying with these essential requirements, however, CMS has exceeded its authority, issuing vague and ill-considered guidance that, as explained above, is infected with errors. Because the guidance cannot be salvaged, and because rulemaking is required, CMS should start over by rescinding its guidance and following the procedures needed to implement the IRA in a responsible and lawful fashion.

Thank you for considering Novo Nordisk's comments. We would be pleased to discuss these comments with you in further detail. If you have questions, please contact Jennifer Duck, VP, Public Affairs at JEDK@novonordisk.com.

April 13, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRARebateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

OMass Therapeutics appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

OMass Therapeutics is preclinical small molecule company based in Oxford in the United Kingdom. To date, we have raised ~\$150M in private financing and will require additional rounds of funding before our products are approved and launch. The US is likely to be one of the largest market for the drugs we are developing, so we have been following the recent developments related to the inflation reduction act with interest and trying to understand what their potential impact on our company strategy may be


Below is a summary on our comments to CMS' Medicare Drug Price Negotiation Program.

- (A) **Section 30.1:** Medicare negotiation for NDA-path drugs at nine-years post-launch
 - a. This disproportionately erodes the investment case for all NDA-path drugs in diseases that affect the elderly or are related to aging
 - b. As a small molecule preclinical company, we believe this provision will have a large impact on our ability to continue to fund our drug discovery platform, as investors and large pharmaceutical companies begin to prefer BLA-path drugs for these types of indications
 - c. For diseases that primarily affect the elderly, small molecules are actually preferred, as they tend to be orals (vs. subcutaneous or IV administration), with a much easier burden of administration- this provision is likely to hamper innovation but also have a detrimental effect on patients
- (B) **Section 30.1.1:** To be considered for the orphan drug exclusion, the drug or biological product must (1) be designated as a drug for only one rare disease or condition under section 526 of the FD&C Act and (2) be approved by the FDA only for one or more indications within such designated rare disease or condition
 - a. As long as a drug remains an orphan drug approved for a single orphan indication, it will be exempt from price negotiation under the IRA. But drugs approved for a second orphan indication under a separate ODD will be subject to negotiation.
 - b. As a company focused on rare diseases, we believe this provision provides perverse incentives and will ultimately reduce the total number of approvals in rare diseases – companies should not be penalized for studying their products in multiple orphan indications

- (C) **Section 50.2:** CMS' processes for determining the Maximum Fair Price for individual medicines as well as the relevance of "therapeutic alternatives" to the drugs it selects for negotiation
- a. Cost-effectiveness math embraced by ICER in the US and other HTA bodies elsewhere (e.g., NICE in the UK) is so simplified that it excludes many demonstrable benefits of medicines (e.g., they liberate caregivers, they reduce risk for healthy people, they go generic yet keep on working), resulting in extreme under-estimations of the value of new medicines. This math can then serve as an excuse for plans to refuse coverage, essentially telling patients that the medicines aren't worth their prices instead of admitting that the plan just doesn't want to pay
 - b. To the extent that CMS wants to appreciate the value that a medicine brings to society before it decides how aggressively to lower its price (particularly in the case of NDA-path drugs that experience negotiation far sooner than would have gone generic), CMS should broadly account for a medicine's value elements, using a dynamic stacked cohort model that accounts for value to patients, to caregivers, and to the rest of the population whose risk is reduced by having the drug (i.e., if it's going to do CEA, do generalized CEA, not conventional over-simplified CEA)
 - c. CMS should consider key product attributes like efficacy, safety, and ease-of-use in determining relevant "therapeutic alternatives" (the basis for CMS' opening bid)
- (D) **Section 40.2.2:** CMS prohibitions on data disclosure and destruction of related documents.
- a. The lack of transparency around the negotiation process makes it impossible for companies to understand which value components CMS is measuring in determining a new price
 - b. Companies need to understand how pricing decisions will be made to inform their clinical development plans and what they need to demonstrate to differentiate their drug vs. competitors
- (E) Additional Comments:
- a. We understand that CMS has stated its guidance in Section 30 is final and that CMS is not seeking or accepting comments on this section
 - b. We recognise that CMS is not permitting comments but we are including these given the significance of the topics incorporated in those sections

We appreciate your considerations of our comments as you develop the Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact me on ros.deegan@omass.com if you have any questions regarding our comments.

Best,

DocuSigned by:

040AB48C9055413...

Ros Deegan



PARTNERSHIP TO FIGHT CHRONIC DISEASE

April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attn: PO Box 8016

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of
Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026

Submitted via email: IRAREbateandNegotiation@cms.hhs.gov

Dear Dr. Seshamani:

The Partnership to Fight Chronic Disease and the 23 undersigned organizations, representing patients, caregivers, providers, and other stakeholders, appreciate the opportunity to share comments, concerns, and opportunities for improving the Medicare Drug Price Negotiation Program: Initial Memorandum.

The Inflation Reduction Act (IRA) of 2022 involves sweeping changes to Medicare including the new Medicare Drug Price Negotiation Program. Given the wide-ranging implications for Medicare beneficiaries today and in the future and the vulnerability of the individuals affected, care to identify and avoid unintended consequences is paramount. These changes also do not occur in a vacuum but are made more complex by challenges with workforce shortages and other access issues that adversely affect many and risk worsening existing health disparities. We urge the Centers for Medicare & Medicaid Services (CMS) to remain vigilant and avoid unintended consequences given the significant changes implementation of the drug negotiation program represents.

Development and implementation of Medicare Drug Price Negotiation Program should accommodate meaningful engagement opportunities for beneficiaries and caregivers.

Given the significance of the changes involved, CMS should seek and allow for more significant and meaningful beneficiary, caregiver, patient, and provider engagement. However, the proposed process and timelines described in the IRA guidance significantly limit those opportunities. When comments are allowed, they involve extremely short timelines for a response. In the guidance, CMS notes that it seeks to include “patient experience” and “factors



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that are of importance to a person”. Additionally, CMS seeks to include evidence, including the consideration of real-world evidence, from “Medicare populations, including on individuals with qualifying disabilities, patients with end-stage renal disease (ESRD), and Medicare-aged populations, as particularly important.”¹ To do so meaningfully, however, allowing sufficient opportunity to analyze the requests, gather evidence to respond, and draft a response takes time.

Given the time, staff, and expertise needed to respond in a timely manner, the short 30-day timeframes for comment will disenfranchise many—particularly those who are already underrepresented and under-resourced. Providing greater transparency in the process and building in more opportunities for engagement, including opportunities to shape data collection, analysis, policy development and ultimately implementation, should be a priority, not just a motion to collect responses to proposed policies. The importance of doing things “right now” should not surpass the importance of doing things “right”. Seeking input on this guidance document instead of allowing for more formal engagement from experts outside of CMS through a more typical proposed rulemaking and comment period, for example, means less input on the program from stakeholders. Further, the 91-page guidance limits areas open for comment and offers a tight timeframe within which the public may comment. These actions are indicative of emphasizing implementation speed over beneficiary impact and public trust.

We urge CMS to consider the proposed process and identify opportunities for public comment and feedback that will not only facilitate implementation of this new program, but more importantly assist CMS in avoiding preventable adverse consequences. For example, though this letter identifies several areas where patient-centric perspectives would enhance the proposed guidance, **the fact that the 91-page guidance does not once mention the health disparities or health equity challenges within Medicare and potential effects of this program is a gross oversight.** That would not have occurred had CMS engaged with patients and beneficiaries earlier in the process.

We are also concerned that the guidance from CMS fails to acknowledge the role of caregivers in supporting patients and the importance of their perspective in the value of treatment they receive. We urge CMS to account for factors that caregivers view as important to them and engage caregivers in the process established in the Drug Price Negotiation Program.

CMS too narrowly defines “unmet medical need.”

Section 1194(e)(2) of the IRA directs CMS to consider evidence of “unmet medical need” of the drug subject to price negotiations and any therapeutic alternatives: “The extent to which the selected drug and the therapeutic alternative to the drug address unmet medical needs for a condition for which treatment or diagnosis is **not addressed adequately by available therapy.**”

¹ Center for Medicare. Medicare Drug Price Negotiation Program: Initial Memorandum. March 15, 2023.



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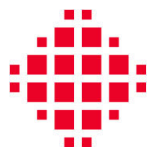
(Emphasis added). In the guidance, CMS states that it “intends to define [unmet medical need] as treating a disease or condition in cases where very limited or no other treatment options exist.” Adequacy, however, is a much different concept than “very limited or no other treatment options.” Adequacy in terms of unmet medical need should be defined more broadly given the heterogeneity of the populations which Medicare serves, the commonality of comorbidities (76% of beneficiaries have three or more chronic conditions), and the significant health disparities that factor into patient need and preference considerations.

The heterogeneity of populations served by Medicare, their needs, and treatment effects should be primary considerations for unmet medical need. Elsewhere in the guidance, CMS notes that information about heterogeneity of treatment affects and the population which CMS plans to consider but ignores “individuals with disabilities, the elderly, individuals who are terminally ill, children, and other patient populations represented among Medicare beneficiaries.” Similarly, the guidance notes that in consideration of clinical benefits, CMS will consider potential risks, harms, or side effects, including “any unique scenarios or considerations related to clinical benefit, safety, and patient experience.” CMS should not ignore those same considerations and the diversity of needs among Medicare beneficiaries as a significant consideration within unmet medical need.

A more robust, patient-centered definition and approach to evaluating unmet medical need is available in the authorizing statute for the Patient-Centered Outcomes Research Institute (PCORI) where federal law requires consideration of the “needs, outcomes and preferences” of patients.² Unmet medical need should incorporate consideration of both the needs and preferences of people living with one or more chronic conditions who may value a treatment with fewer side effects and contraindications. People, particularly those living with disabilities or with limited transportation options or health care access (e.g., in rural areas or care deserts), may need and prefer modes of administration that do not require traveling and involve less frequent administration. A narrow definition of unmet need may also further lead to the undervaluing of communities of color who may have pre-existing health deficits due to numerous inequities including the negative consequences of social determinants of health³ and

² 42 USC Sec 1320e(d)(1)(A)

³ National Snapshots of Social Determinants of Health. HealthyPeople.gov. Available at: <https://www.healthypeople.gov/2020/topics-objectives/topic/social-determinants-of-health/national-snapshot>



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racism,⁴ including reduced access to care,⁵ reduced quality of care,⁶ and higher prevalence of disease and disease-related mortality.⁷

There is also an important opportunity for considering unmet medical need as being more encompassing of patient needs and realities in evaluating the adequacy of existing therapeutic options. In FDA's Guidance for Industry on Expedited Programs for Serious Conditions—Drugs and Biologics, the FDA defines unmet medical need as a “condition whose treatment or diagnosis is not addressed adequately by available therapy.”⁸ FDA further describes a new treatment as addressing an unmet medical need if it, “has an improved effect on a serious outcome(s) of the condition compared with available therapy.”⁹ Other considerations include having “an improved effect on a serious outcome(d) of the condition compared with available therapy,” “has an effect on a serious outcome of the condition in patients who are unable to tolerate or failed to respond to available therapy,” or “provides safety and efficacy comparable to those of available therapy but has a documented benefit, such as improved compliance, that is expected to lead to an improvement in serious outcomes.” None of these factors are captured in CMS's currently proposed definition of “unmet medical need”.

Also, reliance on averages to define unmet medical need misses the needs of subpopulations for whom therapeutic options are more limited because of their health status or considerations of social determinants of health. This is especially relevant for millions managing multiple chronic conditions. For example, research provides evidence of racial and ethnic health disparities in outcomes and prevalence of chronic illness among Medicare beneficiaries. Many report poorer health status, higher rates of ED visits and hospitalizations, but fewer doctor's visits.¹⁰ All of these realities factor into consideration of choice and success of prescription drug regimens, adherence, and outcomes. Failure to consider these factors in unmet medical need may further exacerbate existing health disparities and outcomes for Medicare beneficiaries.

4 Boyd RW, Lindo EG, Weeks LD, McLemore M. On Racism: A New Standard for Publishing on Racial Health Inequities. Health Affairs. 2 July 2020. Available at:

<https://www.healthaffairs.org/doi/10.1377/hblog20200630.939347/full/>

5 Artiga S and Orgera K. Key Facts on Health and Health Care by Race and Ethnicity. Kaiser Family Foundation. 12 Nov 2019. Available at: <https://www.kff.org/report-section/key-facts-on-health-and-health-care-by-race-and-ethnicity-introduction/>

6 2019 National Healthcare Quality and Disparities Report. Content last reviewed June 2021. Agency for Healthcare Research and Quality, Rockville, MD. <https://www.ahrq.gov/research/findings/nhqrdr/nhqrdr19/index.html>

7 Minority Population Profiles. Office of Minority Health. Available at:

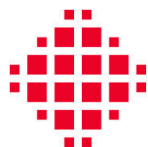
<https://www.minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=26>

8 US Department of Health and Human Services, Food and Drug Administration. Guidance for Industry: Expedited Programs for Serious Conditions—Drugs and Biologics. May 2014. Available at

<https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf>

9 Ibid.

10 Ochieng N, Cubanski J, et al. Racial and Ethnic Health Inequities in Medicare. Kaiser Family Foundation. Feb. 16, 2021. Available at <https://www.kff.org/medicare/report/racial-and-ethnic-health-inequities-and-medicare/#:~:text=Among%20Medicare%20beneficiaries%2C%20people%20of,have%20higher%20rates%20of%20hospital>



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By articulating a clear and patient centered definition of “unmet medical need” CMS has an opportunity to create standards and send signals for the types of medical advances that will support the needs of patients for years to come.

The Quality-Adjusted Life Year (QALY) has no place in the guidance given its inherent bias against older adults and people living with disabilities.

We appreciate CMS’s recognition of the problems with QALYs and pledge to not consider QALYs outside of clinical effectiveness as noted in the IRA Guidance. For a program designed to primarily serve older adults and people living with qualifying disabilities, however, QALYs and evidence based on QALYs should not be a factor for consideration at all. As noted in the seminal report by the National Council on Disabilities, the QALY discriminates against these populations¹¹ and pledges to limit their use do not fully eliminate this reality. The QALY undervalues interventions intended for populations with shorter life spans, which include many of the communities for which CMS has expressed a particular interest: older populations and people living with disabilities, as well as people of color. We strongly encourage CMS to adopt the prohibition of reliance on the QALY in Medicare as required as part of the Affordable Care Act and avoid using either metric in evaluating clinical effectiveness or factoring these metrics into developing a fair maximum price.

CMS should protect patient access beyond requiring coverage.

Coverage does not equate to access. Utilization management techniques including, “fail first” or non-clinical step therapy, and prior authorization erect significant barriers to access for patients. We strongly encourage CMS to monitor benefit design and address potential barriers to access in addition to requiring coverage for drugs subject to the drug pricing program.

We appreciate the complexities involved in implementing this significant shift in Medicare and financing of prescription drug coverage. We also appreciate the opportunity to provide comments we hope will aid implementation in ways that protect and enhance beneficiary access to the medicines they need to maintain and enhance their health. We stand ready to assist in that regard and urge CMS to re-evaluate the proposed process for evaluating drugs and determining pricing to allow for additional, meaningful public input and beneficiary engagement in the process. Please contact Candace DeMatteis, candace.dematteis@fightchronicdisease.org for additional information.

¹¹ National Council on Disabilities. Quality-Adjusted Life Years and the Devaluation of Life with Disability. Nov. 6, 2019. Available at https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf



PARTNERSHIP TO FIGHT CHRONIC DISEASE

Signed,

Alliance for Aging Research
American Behcet's Disease Association (ABDA)
Association of Asian Pacific Community Health Organizations (AAPCHO)
CancerCare
Caregiver Action Network
Chondrosarcoma CS Foundation, Inc.
The COSHAR Healthy Communities Foundation
Derma Care Access Network
Firefly Fund
Headache and Migraine Policy Forum
Healthy Men Inc.
Hereditary Neuropathy Foundation
The Latino Coalition
LUNgevity Foundation
National Kidney Foundation
National Minority Quality Forum
National Oncology State Network (NOSN)
National Puerto Rican Chamber of Commerce
New Jersey Association of Mental Health and Addiction Agencies, Inc.
NTM Info & Research
Partnership to Advance Cardiovascular Health
Partnership to Fight Chronic Disease (PFCD)
South Asian Public Health Association
Stronger Than Sarcoidosis

April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Dear Deputy Administrator Seshamani:

Thank you for this opportunity to comment on the Initial Memorandum for Implementation of the Medicare Drug Price Negotiation Program. Our organizations represent the public stakeholders referenced in the guidance – the patients and people with disabilities impacted by this negotiation process. Our comments will focus on the role that we hope to play in ensuring that the agency centers its considerations on outcomes that matter to patients and people with disabilities as it implements this important new program to ensure drug affordability for individuals under Medicare.

The Maximum Fair Price (MFP) provisions of the Inflation Reduction Act (IRA) provide the Centers for Medicare & Medicaid Services (CMS) with significant new authority to reduce drug prices for Medicare beneficiaries. As your guidance recognized, the MFP provisions of the law also include provisions to protect patients and support patient centered action. CMS has the opportunity to continue advancing this crucial goal throughout the implementation of the Medicare Drug Price Negotiation Program. As CMS makes decisions to improve drug affordability, it is vital for the agency to center its decisions around patients and people with disabilities.

Specifically, this important new program gives CMS an opportunity to advance patient-centeredness in health care decision making while improving medical affordability through lower drug prices. While we commend the agency for the steps it has already taken in this direction, such as soliciting stakeholder input at the beginning of the decision-making process, we urge the agency to include additional measures to ensure the program is truly centered on the needs of patients and people with disabilities.

Our recommendations below center on three pillars: 1) creating additional procedures to meaningfully engage with patients and ensure that the evidence CMS relies on is transparent; 2) establishing patient-centered standards and outcomes; and 3) more definitively rejecting the use of Quality-Adjusted Life Years (QALYs) and other discriminatory cost-effectiveness standards. We believe these recommendations will be useful to CMS in developing evidentiary standards and engagement practices that ensure patient benefits are central to decision-making.

We Urge Meaningful Engagement of Patients and People with Disabilities

Allowing members of the public to provide input into the decision-making process, particularly the Medicare beneficiaries directly impacted by this work, will best position CMS to identify all available unbiased and nondiscriminatory evidence for the factors described in section 1194(e)(2). We appreciate that CMS is inviting patients and other public stakeholders to provide input in an initial 30-day period for information collection. Further, we are aware that CMS also released an information collection request (ICR) on Negotiation Data Elements which describes how CMS intends to collect the data described, including information relevant to section 1194(e)(2). We are reviewing this and will provide additional comments as pertinent. As CMS considers the tactics that will be used to gather information, we provide the following recommendations:

- CMS should create an **ombudsman** for the Medicare Drug Price Negotiation Program to act as a central point of input for patients and people with disabilities, similar to the Food & Drug Administration's (FDA's) Patient Affairs Office or the Patient-Centered Outcomes Research Institute's (PCORI's) Director of Patient Engagement. The ombudsman should be an individual with significant experience in patient engagement, familiar with the organizations representing patients and people with disabilities and responsible for ensuring that input is disseminated to decision-makers at CMS and responses are given back to those providing said input.
- ***CMS should incorporate additional procedures to obtain and respond to input from patients and people with disabilities early*** in the drug price negotiation process, giving stakeholders time to collect and provide meaningful comments. CMS likely will need to begin seeking input from patients and caregivers very early in the process so that CMS can consider it along with other inputs before the agency makes an "initial offer" of a Maximum Fair Price. This should go beyond written comments provided through a single, open-ended Information Collection Request, and could include, for example, CMS convening ***public roundtables*** of disease or treatment-specific experts from the patient and disability communities, as well as their caregivers, for each drug selected for MFP negotiation.
 - This process should look similar to the process used by the FDA to engage patients as part of Patient-Focused Drug Development, both as part of externally led meetings¹ and FDA-led meetings.²
 - Another potential reference point is the engagement process used by PCORI to identify the outcomes that the organization values. CMS should similarly engage patients and people with disabilities to establish a predictable process for engagement related to its consideration of data elements about a selected drug, the

¹ "Externally-Led Patient-Focused Drug Development Meetings." U.S. Food and Drug Administration, FDA, 29 July 2022, <https://www.fda.gov/industry/prescription-drug-user-fee-amendments/externally-led-patient-focused-drug-development-meetings>

² "Externally-Led Patient-Focused Drug Development Meetings." U.S. Food and Drug Administration, FDA, 29 July 2022, <https://www.fda.gov/industry/prescription-drug-user-fee-amendments/externally-led-patient-focused-drug-development-meetings>

evidence used in consideration of factors in statute used to assess therapeutic value, and its alternative therapies.

- CMS should share the non-proprietary evidence that they are considering for unmet need, including comparative research and therapeutic advance. The agency should then solicit feedback about its relevance to the needs, and outcomes and preferences of patients. CMS should also solicit other patient sources from patients and people with disabilities that may have their own resources for collecting data.
- CMS should solicit input from **diverse** communities, in order to gain information about the differences among subpopulations and their needs, outcomes, and preferences.
- CMS should provide patients and people with disabilities the **resources needed for effective engagement**.
 - Resources may include providing financial assistance to facilitate participation in meetings and roundtables, making meetings accessible to people with disabilities, providing informational materials in accessible formats, funding surveys and other forms of real-world evidence generation, and/or allowing an extended amount of time for input and comments.
 - This recommendation is consistent with best practices supporting engagement, particularly supporting the engagement of those historically not engaged, as consistently reflected in the work of PCORI.³
- CMS should **seek input on topics that are relevant to people with disabilities, patients, and caregivers**, and should clearly describe these topics to these stakeholders in advance. This engagement could include, for example, feedback on relevant treatment alternatives, outcomes that matter to patients, and the relative importance of these outcomes.
- CMS decisions should be **sufficiently transparent** so that people with disabilities, patients, and caregivers can see the extent to which their input was considered in the agency's decisions, ideally during the deliberation process before a final decision is made.
- CMS should **ensure that information gathered during public comment periods and meetings is reflected in the final guidance** that CMS publishes in advance of the first year of negotiations, advancing the principle of transparency that is supported across organizations.

³ PCORI, "Financial Compensation of Patients, Caregivers, And Patient/Caregiver Organizations Engaged in Pcori-Funded Research as Engaged Research Partners," Patient-Centered Outcomes Research Institute, published June 10, 2015, <https://www.pcori.org/sites/default/files/PCORI-Compensation-Framework-for-Engaged-Research-Partners.pdf>.

- CMS should engage patients and people with disabilities ***to assess any unintended consequences***, including the impact on access to treatment, cost-sharing implications, or otherwise.
 - Organizations such as the Partnership to Improve Patient Care,⁴ the National Council on Disability (NCD),⁵ and the Disability Rights Education and Defense Fund (DREDF)⁶ have identified restricted access implications experienced in countries relying on methods for assessing value that fail to capture the real-world value to patients.

We urge CMS to Explicitly Recognize, Without Exception, the Existing Statute Barring Use of QALYs and Similar Measures, Consistent with Current Law and Recommendations of the National Council on Disability Against Reliance on Cost-Effectiveness.

The initial CMS guidance recognized the agency’s authorization to consider evidence about the selected drug, including whether the selected drug represents a therapeutic advance, its alternatives, comparative effectiveness and effects on specific subpopulations, and extent to which unmet medical needs are addressed. This reflects the IRA’s focus on driving significant discounts in drug prices through the use of comparative clinical effectiveness research and cost data vs. one-size-fits-all cost-effectiveness analyses, consistent with the concerns of the NCD^{7, 8} and other disability rights organizations.^{9, 10}

CMS acknowledged that the agency may not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. However, the initial CMS guidance did not reference

⁴ Partnership to Improve Patient Care, PIPC, <http://www.pipcpatients.org/international.html>

⁵ National Council on Disability. (November 16, 2019). Quality-Adjusted Life Years and the Devaluation of Life with Disability. https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

⁶ DREDF, ICER Analyses Based on the QALY Violate Disability Nondiscrimination Law , September 21, 2021 at <https://dredf.org/wp-content/uploads/2021/09/ICER-Analyses-Based-on-the-QALY-Violate-Disability-Nondiscrimination-Law-9-17-2021.pdf>

⁷ The NCD recommended that Congress, “Avoid creating provisions of any bill that would require the agency with management and oversight responsibilities (such as, for example, HHS) to cover only the most cost-effective drugs and treatments, or to require the agency to impose restrictions on less cost-effective treatments.” https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

⁸ The NCD recommended Medicaid guidance, “The guidance should specifically discuss how these authorities apply to benefits and reimbursement decisions, and that payment decisions should not rely on cost-effectiveness research or reports that are developed using QALYs.” https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

⁹ Joint letter from advocates to Oregon HERC, “Most cost-effectiveness analyses rely on data from randomized clinical trials (RCTs) and health utility preference weighting surveys, data sources that primarily rely on inputs from non-disabled, white, Caucasian populations. This systematically biases available therapies to favor covering those that are effective for white people to the detriment of covering treatments effective for people of color and people with disabilities.” http://www.pipcpatients.org/uploads/1/2/9/0/12902828/herc_letter.pdf

¹⁰ Joint letter to CMS, October 23, 2022, “More broadly, we also support the NCD recommendation that federal programs, including Medicaid, should not rely on cost-effectiveness research or reports that gather input from the public on health preferences that do not include the input of people with disabilities and chronic illnesses.”

the Affordable Care Act (ACA) which specifically bars the use of the QALY and includes the language, “The Secretary shall not utilize such an adjusted life year (or such a similar measure) as a threshold to determine coverage, reimbursement, or incentive programs under title XVIII.”¹¹

We deeply appreciate the statement made by Secretary Becerra on March 29, 2023, reaffirming that CMS will not use QALYs or similar measures, and look forward to the agency strengthening its guidance to reaffirm this.¹² We urge CMS to use language in its final guidance clarifying that existing law bars the use of QALYs and similar measures, not just QALYs as used in the context of life extension, and to state explicitly that, as directed in the IRA, it will rely on the factors of comparative clinical effectiveness outlined in section 1194(e)(2).

At a recent hearing in the House Energy and Commerce Committee, Ranking Member Frank Pallone, a primary author of the Inflation Reduction Act’s health care provisions, stated that the Congress had passed a landmark law allowing for Medicare Drug Price Negotiation “while also explicitly prohibiting the use of QALYs in this process.”¹³ The ACA passed in 2010 and barred Medicare from using QALYs and similar metrics throughout Medicare, including the drug negotiation process. The IRA went a step further, ensuring that no evidence would be considered that valued life extension for older adults, people with disabilities, and people at the end of life as less than their counterparts, which Ranking Member Pallone and others have recognized to include QALYs.¹⁴

Therefore, we urge CMS to provide clarity that its drug negotiation process will be grounded in evaluation of comparative clinical effectiveness and patient-centered health outcomes and not use or consider QALYs or other cost-effectiveness standards that frequently discriminate against subgroups and devalue the needs and preferences of patients. This includes biased non-QALY measures such as the Equal Value of Life Years Gained (evLYG), a metric recently created by the Institute for Clinical and Economic Review (ICER) to supplement the QALY that similarly discriminates based on age and has shortcomings in accounting for quality-of-life improvements.¹⁵ The NCD and DREDF have each analyzed the QALY and the evLYG to conclude neither are suitable measures for assessing treatments.

¹¹ House of Representatives, Congress. 42 U.S.C. 1320e - Comparative clinical effectiveness research. U.S. Government Publishing Office, <https://www.govinfo.gov/app/details/USCODE-2010-title42/USCODE-2010-title42-chap7-subchapXI-partD-sec1320e>

¹² “Health Subcommittee Hearing: ‘Fiscal Year 2024 Department of Health and Human Services Budget.’” YouTube, 29 March 2023, <https://youtu.be/OPMG5OU0I6c>.

¹³ “Health Subcommittee Legislative Hearing (Lives Worth Living).” YouTube, 1 Feb. 2023, https://www.youtube.com/watch?v=IzE_DVqg6dk.

¹⁴ Ranking Member Anna Eshoo stated, “Democrats included a ban on QALYs in Medicare and the Affordable Care Act in 2010. Last year, Democrats further clarified that QALYs could not be used as part of Medicare’s prescription drug price negotiations in the IRA.” “Full Committee Markup of 19 Bills (Part 2),” 24 March 2023.

¹⁵ “Cost-Effectiveness, the QALY, and the Evlyg.” ICER, Institute for Clinical and Economic Review, 28 Mar. 2023, <https://icer.org/our-approach/methods-process/cost-effectiveness-the-qaly-and-the-evlyg/>

Recommendation:

- CMS should ***clarify in guidance and/or regulations that it will not use or consider QALYs or similar measures in any way.***
 - This recommendation is consistent with ACA’s statutory ban on the use of QALYs and similar measures in coverage, reimbursement, and incentive programs in Medicare decisions.
 - This recommendation would also uphold the IRA’s requirement that the comparative clinical effectiveness research factored into determinations of therapeutic benefit do not discriminate.
- With regard to CMS solicitation of information on other specific measures that discriminate, ***CMS should avoid consideration of any evidence that is informed by QALYs or similar measures such as the evLYG^{16 17} or Disability Adjusted Life Years (DALYs).^{18,19}***

Consideration of Non-QALY Evidence in Reports Using QALYs

While we appreciate CMS’s assurance that it will not consider QALYs, we are concerned that the guidance leaves the door open to submission of QALY-based analysis within other clinical or cost-effectiveness assessments. We urge transparency in how these assessments are ultimately used by the agency.

It is important to understand that most of the components that make up the calculation of QALY estimates may also be used in a particular study’s assessment of comparative clinical

¹⁶ The NCD described the eLYG in its report as, "There are other challenges to the evLYG that indicate that it is not a suitable alternative to the QALY. First, as evidenced by the assessment of Spinraza, denial of coverage is possible under the QALY/evLYG system, even where a drug would provide significant clinical benefit, including life extension. Second, the QALY/evLYG system still relies on health utility weights to measure quality of life improvements, despite the fact that such measures are typically derived from survey data and do not account for the complexity of the preferences and experiences of people with disabilities. Third, the QALY/evLYG system affords no opportunity to account for clinical knowledge not reflected in the research literature, a significant concern articulated in Chapter 1. Finally, even within the narrow emphasis on life extension, ICER provides no guidance to payers as to which reimbursement level to prioritize—the one derived from the QALY or the one derived from the evLYG." https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

¹⁷ DREDF concluded the following about evLYG, "Thus, adding the evLYG is not a solution; it merely forces payers to choose between one measure that undervalues life extension (the QALY) and one that affords no value to quality of life improvements (the evLYG). Neither account for both the full value of life-extension and the value of quality-of-life improvement." <https://dredf.org/wp-content/uploads/2021/09/ICER-Analyses-Based-on-the-QALY-Violate-Disability-Nondiscrimination-Law-9-17-2021.pdf>

¹⁸ Coelho, Tony. "PCORI Comments on Value Letter." Received by Dr. Nakela Cook, 3 Mar. 2023. http://www.pipcpatients.org/uploads/1/2/9/0/12902828/pcori_comments_on_value.pdf

¹⁹ Grosse, Scott D et al. "Disability and disability-adjusted life years: not the same." Public health reports (Washington, D.C. : 1974) vol. 124,2 (2009): 197-202. doi:10.1177/003335490912400206

effectiveness and therefore could be subject to the same biases inherent in the QALY totals themselves. Simply cherry-picking the components of these QALY estimates that are included a study of comparative clinical effectiveness is not an effective route to avoiding their biases.

Instead, we urge CMS to identify with greater detail and transparency the acceptable input data variables to be taken from comparative clinical effectiveness research, in order to ensure that the methods used will not result in bias against older adults, people with disabilities, and people at the end of life. For example, CMS should recognize that the use of value or utility weights in comparative clinical effectiveness research may also be used in the QALY calculation and therefore also subject to bias and validity challenges.²⁰ These weights are often constructed by a very small subgroup of a country's population²¹ despite purporting to represent all.²² Yet, there is considerable empirical evidence that treatments impact people differently and that society strongly disagrees with treating all conditions, disease states, and patient types with the same priority.^{23,24}

The QALY can introduce bias into a study of a treatment's effectiveness in several ways. For example, life expectancy estimates for the population being treated may be calculated from an older population or from a population that has co-existing conditions or disabilities, thereby creating weights for the potential life year gains that could accrue to a successfully treated individual that give a biased view of life-years gained. Another example is the quality of life (QOL) part of the equation - the source data for the weights that turn life years into quality-adjusted life years. We are concerned that the patient-reported outcome measures (PROs) in the commonly used EuroQoL instrument (EQ-5D) do not meet the FDA's definition:

*PRO instrument item generation is incomplete without a range of patients with the condition of interest to represent appropriate variations in severity and in population characteristics such as age or sex.*²⁵

The EQ-5D is the most commonly used PRO within QALY calculations, yet it relies upon weightings constructed by populations unfamiliar with the conditions being evaluated and therefore does not have the accuracy that is obtained by consulting with patients. Recent studies have provided strong evidence to suggest that there is a public bias against people with

²⁰ Smith S, Cano S, Browne J. "Patient reported outcome measurement: drawbacks of existing methods". *bmj*. 2019 Feb 27;364:l844.

²¹ McClimans L, Browne JP. "Quality of life is a process not an outcome. Theoretical medicine and bioethics". 2012 Aug 1;33(4):279-92.

²² Broome J. "Fairness Versus Doing the Most Good". *The Hastings Center Report*. 1994 Jul 1;24(4):36-9.

²³ Weinstein MC. "A QALY is a QALY is a QALY—or is it?" *Journal of Health Economics*. July 1988 289-291.

²⁴ Whitehead SJ, Ali S. "Health outcomes in economic evaluation: the QALY and utilities". *British medical bulletin*. 2010 Dec 1;96(1):5-21.

²⁵ US Food and Drug Administration "Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims". 2009. [2020-07-15].

disabilities.²⁶ Criticism of the inherent bias of the EQ-5D is widespread and growing.^{27,28} It is also widely critiqued for failing to represent any consensus about the value of health states, as surveys of the general public reveal enormous heterogeneity (i.e., disagreement) within surveyed populations.²⁹

Selective use of QALYs or selective use of the components of data inputs that make up QALY calculations in studies of comparative clinical effectiveness raise many of the same dangers as the blanket use of QALYs for measuring the therapeutic benefit or “value” of a drug to a patient or to society. The biases that CMS emphasizes that it needs to avoid are built into the methodological construction of QALYs at multiple levels. Attempts by CMS to pick their way around these biases by selectively choosing components of QALY estimates where convenient would have significant risks for bias and discrimination.

Recommendation:

- CMS should clarify in the final guidance that ***evidence relying on the same biased or discriminatory inputs, particularly the value sets or weights used to measure life extension or quality of life, will not be relied on*** as evidence for the factors of therapeutic benefit that CMS is authorized to consider in section 1194(e)(2).

Consideration of Comparative Clinical Effectiveness Research and Appropriate Comparators

We appreciate that CMS clearly states in its guidance its intent to consider “health outcomes, intermediate outcomes, surrogate endpoints, patient-reported outcomes, and patient experience when reviewing the clinical benefit of the selected drug and its therapeutic alternative(s).” As directed by current law, this includes a bar on any use of the QALY. We strongly urge CMS to directly engage affected stakeholders – the patients, people with disabilities and clinicians with practicing experience in the condition being treated – as the experts in determining the therapeutic benefit of treatments based on outcomes that are valued by patients.

Recommendations:

- ***CMS should clearly define comparative clinical effectiveness research*** in a manner consistent with the existing definition in the ACA.

²⁶ HJ, Chaudhry. “Expanding Licensure Portability and Access to Care: Lessons Learned during Covid-19.” Health Affairs (Project Hope), U.S. National Library of Medicine, <https://pubmed.ncbi.nlm.nih.gov/35914196/>

²⁷ Cubi-Molla P, Shah K, Burström K. “Experience-Based Values: A Framework for Classifying Different Types of Experience in Health Valuation Research”. *Patient*. 2018 Jun;11(3):253–270.

²⁸ Helgesson G, Ernstsson O, Åström M, Burström K. “Whom should we ask? A systematic literature review of the arguments regarding the most accurate source of information for valuation of health states”. *Qual Life Res*. 2020 Jul;29(6):1465–1482

²⁹ Bansback N, Tsuchiya A, Brazier J, Anis A. “Canadian valuation of EQ-5D health states: preliminary value set and considerations for future valuation studies”. *PLoS One*. 2012;7:e31115.

- The ACA stated, “The terms ‘comparative clinical effectiveness research’ and ‘research’ mean research evaluating and comparing health outcomes and the clinical effectiveness, risks, and benefits of 2 or more medical treatments, services, and items...” and makes it clear that such research does not involve cost comparisons or cost-effectiveness.
- In determining what comparative clinical effectiveness research to rely on, CMS should consider engaging patients and people with disabilities to understand their perspectives on the quality of the research available and whether it represents their preferred outcomes and experiences.
- The comparator matters and should reflect a clinically comparable treatment as indicated by patients and their clinicians as opposed to selecting a comparator based on its cost, a lesson learned from countries such as Germany and a key component of efforts to advance innovative methods.³⁰ We do not recommend that the initial offer rely solely on the price of a therapeutic alternative, but instead reflect the negotiated drug’s therapeutic benefit.

Therapeutic Advance and Unmet Need

We appreciate that CMS specifically stated its intention to review real-world evidence. Data generated by registries and other sources of real-world data, particularly for subpopulations such as people with disabilities, should be treated as highly relevant to the factors listed in section 1194(e)(2) as they provide current evidence of the experience of patients that may not yet be reflected in other research literature or clinical trial data. When developing its offer for MFPs, CMS should ensure it is prioritizing feedback from patients, people with disabilities, and clinicians with practicing experience with the condition, as well as assessments of therapeutic benefit, thereby considering value through the lens of how patients and people with disabilities experience and value their health care. Doing so will require a strong commitment to engagement.³¹

Recommendations:

- CMS should determine whether a treatment reflects a ***therapeutic advance*** based not only on the clinical trial data but also on evidence that reflects what patients and people with disabilities value about their care and outcomes.
 - CMS will need to engage specific patient and disability communities with the condition treated by a selected drug to determine their specific priorities for

³⁰ PIPC, “The German Health Care System and its Impact on Patient Access – Lessons for the U.S., http://www.pipcpatients.org/uploads/1/2/9/0/12902828/germany_draft_2022_9-21_edited_clean.pdf

³¹ Smith, Theo. “Real-World Evidence Classroom.” National Health Council, 28 Feb. 2023, <https://nationalhealthcouncil.org/additional-resources/real-world-evidence-classroom/>

improving their quality of life with treatment, a theme consistent in calls for improved patient engagement in research and decision-making.^{32,33}

- CMS should specifically call for studies related to therapeutic advancements that reflect the diversity of the patients being treated.^{34,35}
- CMS should define **unmet need** based on the patient perspective and whether a treatment meets their needs, outcomes, and preferences in a manner unmet by other treatments, consistent with the PCORI's statutory charge to address the “needs, outcomes and preferences” of patients.³⁶
 - Unmet need should be defined in a manner that acknowledges the experiences of people living with a condition who may value a treatment with fewer side effects, modes of administration that do not require travel, frequency of administration, etc. The CMS definition should prioritize how a treatment advances adherence and improved quality-of-life as indicated by engaging patients and people with disabilities and by use of patient-level data.
 - Unmet need should not be defined by the averages, but instead take into consideration the subpopulations that may not benefit from existing therapies due to their unique characteristics or for whom those therapies are not accessible due to social determinants of health (SDOH).

CMS Should Set a High Bar for the Quality of Evidence to be Considered.

CMS stated its intent to consider the “source, rigor of the study methodology, current relevance to the selected drug and its therapeutic alternative(s), whether the study has been through peer review, study limitations, degree of certainty of conclusions, risk of bias, study time horizons, generalizability, study population, and relevance to the negotiation factors listed

³² PCORI, “Engagement Rubric for Applicants,” *Patient-Centered Outcomes Research Institute*, last modified June 6, 2016, <https://www.pcori.org/sites/default/files/Engagement-Rubric.pdf>.

³³ NCD recommended, “HHS should consider including explicitly recruiting people with disabilities and chronic illnesses as members of committees and working groups formed to develop effective healthcare reform and strategies for lowering the cost of prescription drugs.”
https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

³⁴ Wartman, Gretchen C, et al. Aligning Health Technology Assessment with Efforts to Advance Health Equity. Partnership to Improve Patient Care,
http://www.pipcpatients.org/uploads/1/2/9/0/12902828/pipc_white_paper_-_measuring_value_in_medicine_-_uses_and_misuses_of_the_qaly.pdf

³⁵ Mark Linthicum, MPP, et al, “Finding Equity in Value: Racial and Health Equity Implications of U.S. HTA Processes,” published 2022, https://sickcells.org/wp-content/uploads/2022/10/IVI_Sick-Cells_Equity-in-Value_2022.pdf

³⁶ House of Representatives, Congress. 42 U.S.C. 1320e - Comparative clinical effectiveness research. U.S. Government Publishing Office, , <https://www.govinfo.gov/app/details/USCODE-2010-title42/USCODE-2010-title42-chap7-subchapXI-partD-sec1320e>

in section 1194(e)(2) of the Act to ensure the integrity of the contributing data within the negotiation process.” CMS has also stated its intent to incorporate real-world evidence into its considerations. We urge CMS to prioritize research that is rigorous, as well as real-world feedback from patients, people with disabilities, and practicing clinicians. Randomized clinical trials and studies relying on the existing literature to make conclusions about the effectiveness of drugs should themselves be peer reviewed and rigorous. It is also important to recognize that real-world evidence from the lived experience of patients, people with disabilities, and clinicians may be observational but is nonetheless also relevant to understanding the impact of treatments that may not have been subject to recent rigorous clinical trials. It will be important for CMS to have high standards that drive the rigorous study of therapeutic benefits in a manner that captures the diversity of people on treatment, the differences among subpopulations, and a focus on outcomes that are valued by patients as communicated to CMS by patients, people with disabilities, and practicing clinicians.

Recommendations:

- CMS should set standards for high-quality, patient-centered evidence that will drive investment in the development and testing of innovative methodologies that are inclusive and advance health equity.
 - Standards established by CMS should recognize and address the ***shortcomings of historic methods that are biased or discriminatory***.
 - CMS should rely on ***standards developed by leading patient and disability organizations*** to determine whether the evidence that it intends to rely on for the development of an initial MFP offer is centered on patients and people with disabilities.^{37,38}
 - To determine what evidence meets standards for quality and patient-centeredness, the agency ***should look to the organizations representing affected patients and people with disabilities as well as the clinical experts*** among practicing physicians and providers, as they would be most familiar with the usefulness of the evidence base for making decisions and its potentially inherent biases.
 - As previously stated, CMS should ***prioritize evidence that is patient-centered*** and captures value for patients, caregivers, and persons with disabilities.

Conclusion

We appreciate CMS’ consideration of our recommendations. CMS has an important task ahead in setting up a process to implement the negotiation provisions of the IRA. For CMS to meet its

³⁷ The Patient Voice in Value - National Health Council. National Health Council, <https://nationalhealthcouncil.org/wp-content/uploads/2020/11/20160328-NHC-Value-Model-Rubric-final.pdf>

³⁸ “Landscape Review and Summary of Patient and Stakeholder Perspectives on Value in Health and Health Care.” PCORI, Patient-Centered Outcomes Research Institute, 2 Sept. 2022, <https://www.pcori.org/resources/landscape-review-and-summary-patient-and-stakeholder-perspectives-value-health-and-health-care>

obligations to beneficiaries, it will be critically important for CMS to be thoughtful in how it assesses therapeutic benefit to affected patients. CMS must ensure that patients and people with disabilities are granted a seat at the table and a clear and robust path to engagement throughout the process.

Sincerely,

Access Ready
Alliance for Aging Research
Alliance for Patient Access
Allies for Independence
ALS Association
American Association of People with Disabilities
American Association on Health and Disability
American Behcet's Disease Association (ABDA)
Asthma and Allergy Foundation of America
Bazelon Center for Mental Health Law
Cancer Support Community
CancerCare
Caring Ambassadors Program
Center for Autism and Related Disorders
Center for Independence of the Disabled, NY
Coalition of State Rheumatology Organizations
Coalition of Texans with Disabilities
Color of Crohn's and Chronic Illness (COCCI)
Cutaneous Lymphoma Foundation
Cystic Fibrosis Research Institute
Davis Phinney Foundation for Parkinson's
Derma Care Access Network
Disability Rights Education and Defense Fund
Disability Rights Oregon
Epilepsy Alliance America
Epilepsy Foundation
Global Liver Institute
Healthy Men Inc.
Hereditary Neuropathy Foundation
ICAN, International Cancer Advocacy Network
Independent Women's Forum
Infusion Access Foundation
Lakeshore Foundation
Lupus and Allied Diseases Association, Inc.
Lupus Foundation of America
MLD Foundation
Multiple Sclerosis Foundation

National Association of Councils on Developmental Disabilities
National Association of Nutrition and Aging Services Programs
National Disability Rights Network (NDRN)
National Down Syndrome Congress
National Down Syndrome Society
National Oncology State Network
New Jersey Association of Mental Health and Addiction Agencies, Inc.
Partnership to Advance Cardiovascular Health
Partnership to Improve Patient Care
Patients Rising Now
RetireSafe
Rosie Bartel
Spondylitis Association of America
The Bonnell Foundation: Living with Cystic Fibrosis
The Coelho Center for Disability Law, Policy and Innovation
The Headache & Migraine Policy Forum
The Hepatitis C Mentor and Support Group-HCMSG
TSC Alliance
United Spinal Association

April 14, 2023

Dr. Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator, Director of the Center for Medicare
Centers for Medicare & Medicaid Services
200 Independence Avenue SW
Washington, DC 20201

Dear Dr. Seshamani,

The undersigned organizations representing a variety of individuals including survivors, and caregivers impacted by cancer diagnoses would like to thank you for the opportunity to provide comments on proposed guidance implementing provisions in the Inflation Reduction Act (IRA). We applaud Congress and the administration for passing and implementing policy to assist individuals who struggle to afford lifesaving and life-enhancing care. However, like many other stakeholders, we also have concerns that some of these policy changes may have unintended negative consequences.

Centers for Medicare & Medicaid Services (CMS) has the opportunity, now, to implement the IRA in such a way that many of these externalities can be prevented. Equally important, however, CMS also has the opportunity to articulate how it will benchmark and assess implementation and monitor its impact on insurance premiums, industry investments, and development of new therapies. In failing to set up an infrastructure to evaluate down-stream impacts, CMS is inviting the worst. The patient community cannot afford to wait for regulators to notice that the patient community is struggling. We have to equip ourselves with the right tools, now, to ensure everyone is kept safe.

Because the IRA is being implemented through sub-regulatory guidance, CMS will have the opportunity to offer timely corrections before unintended downstream consequences and accidental loopholes become permanent features of these new policies. This will only work if CMS sets up the infrastructure to collect that feedback and act on it in a timely manner. As we have seen with policies like prior authorization in the Medicare Advantage program, adjusting or clarifying existing policy after it is already firmly in place, can be difficult, if not impossible to accomplish.

Drug Price Negotiations

In this guidance, CMS outlines a plan for how drug prices will be negotiated. In separate guidance, CMS explains how it will evaluate a drug's "clinical benefit." However, neither of these documents demonstrate how patient needs will be incorporated in this process. It makes sense that the needs of patients and caregivers will change over time, and it makes sense that two individuals might experience the same events in entirely different ways, yet policy consistently dictates that patient feedback is static and standardized.

CMS must use this opportunity to build a new system that acknowledges and responds to these truths. ***To be clear: asking for comment letters at this stage and allowing for submission of evidence once drugs have been selected for negotiation is not enough.*** Patients must have the opportunity to share their care preferences, impacts on quality of life, and what they value about our treatment.

- 1) We call on CMS to host a town hall meeting with patient stakeholders prior to finalizing guidance to inform how CMS will establish the definition of clinical benefit used in drug price negotiations and discuss the infrastructure for continuing patient engagement.**

- 2) **We respectfully ask that CMS consider the following:**
 - a. **For each drug assessed, a panel of patients and caregivers should be convened to provide input and feedback at multiple steps in the evaluation of a drug's benefits. There should be an open and transparent process for patients and caregivers to apply to be part of these panels.**
 - b. **Patient input should not just be considered qualitative and described in written form. Rather, it should be quantified and incorporated into any methodology used to assess product value.**
 - c. **CMS should be transparent and clearly outline how patient input was considered and impacted the negotiation process.**
- 3) **We endorse recommendations explained in more detail in the patient- and disability-community letter penned by the Partnership to Improve Patient Care (PIPC).**

Patient Access

According to the recent guidance, Medicare Part D plans shall include each covered Part D drug that is a selected drug on Part D formularies during Contract Year (CY) 2026 and all subsequent years for which the MFP of the selected drug is in effect during the price applicability period. While patient groups are optimistic that these changes will allow patients to afford needed treatments, we remain cautious. Historically, health plans have used creative formulary design, onerous prior authorization schemes, and step therapy delays to limit plan liabilities, all of which adversely affect patient access to medicines. We are disappointed that CMS did not proactively address these patient access concerns in the guidance. We are also concerned that without appropriate guardrails and patient protections on utilization management, health plans will expand their inappropriate overutilization of these tools to recoup their perceived losses.

We urge CMS to ensure that health plan utilization management techniques follow clinical guidelines, provide timely and transparent responses to patients, and allow for physician/patient choice based on individual patient medical needs and desired outcomes. In addition, we urge CMS to establish a feedback mechanism to monitor overutilization of these cost control tools, particularly as they apply to Part D drugs subject to this policy. CMS must also proactively address how Part D redesign changes will impact patient access to both negotiated and non-negotiated cures.

Out of Pocket Caps

The IRA caps the out-of-pocket costs paid annually by Medicare beneficiaries for prescription drugs at \$2,000 and allows patients to spread those costs across 12 months through a "smoothing" mechanism. The redesign also eliminates the coverage gap discount program. If implemented correctly, and in collaboration with patient advocacy organizations like those included on this letter, these policies could help to deliver essential treatments to Medicare beneficiaries and help them avoid the financial toxicity that frequently accompanies a cancer diagnosis. **CMS must invest in education and assistance programs to ensure that they are well understood.** We stand ready to help CMS to build education tools, assist in education, and outreach efforts to ensure that the smoothing process does not end up adding to more confusion and unexpected and compounded healthcare debt.

The Impact to Oncology Research and Development

The IRA allows Medicare to set prices on small molecule drugs after they have been on the market for nine years. That is much shorter than the 13-year window granted to large molecule "biologic" drugs,

which are typically injected or infused in doctors' offices, clinics, and hospitals and are subject to Medicare Part B.

Clinical trials are resource-intensive endeavors that take years to complete. The trials that drug developers run to assess whether an FDA-approved drug can be used to treat an earlier stage of a disease, in combination with another therapy, or in a different cancer type or population, can take more than three years to finish on average. Over 60 percent of oncology drugs approved between 2010-2012 received an additional FDA indication, and more than 70 percent of these additional approvals occurred seven or more years after initial approval.¹ We are concerned that pharmaceutical companies will determine that it is not viable to invest in clinical research supporting approval for additional indications if they cannot count on the same return – which can only limit treatment options for patients who might have otherwise benefitted from existing, sound, and life-saving or life-improving science.

CMS must articulate how it will monitor industry investment and drug development and this plan has to provide an opportunity for patient engagement. None of us can afford to watch lifesaving or life-enhancing treatments languish.

This year, nearly two million Americans will be diagnosed with cancer.² Life-saving treatments for some of those patients may already be on the market. But the IRA's timelines could prevent scientists and doctors from discovering new uses for those already-approved drugs. Since 1991, the cancer death rate has declined by 33 percent.³ This is in large part due to advances in treatment.

While the passage and implementation of IRA represents a positive step for patients and caregivers, the opportunity for negative consequences demands that CMS establish an infrastructure that monitors predicted trends and ensures the opportunity for feedback. We are ready and eager to assist in this process and look forward to collaboration. Please contact Courtney Yohe Savage, MPP at cysavage@cancersupportcommunity.org or 202-680-8985 with any questions or follow-up.

Sincerely,

Cancer Support Community
Association of Community Cancer Centers
Bladder Cancer Advocacy Network (BCAN)
COA Patient Advocacy Network (CPAN)
Community Oncology Alliance (COA)
Global Coalition on Aging Alliance for Health Innovation
Global Liver Institute
HealthHIV
National Oncology State Network

¹ <https://www.pharllc.com/wp-content/uploads/2022/11/Clinical-Benefits-of-Post-Authorization-Research-Brief.pdf>

² <https://pubmed.ncbi.nlm.nih.gov/36633525/#:~:text=In%202023%2C%201%2C958%2C310%20new%20cancer,occur%20in%20the%20United%20States.>

³ <https://www.fiercehealthcare.com/providers/study-finds-cancer-death-rate-declined-33-1991-treatment-advances>

Meena Seshamani, M.D., Ph.D.

April 14, 2023

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Ovarian Cancer Research Alliance
Partnership to Improve Patient Care
Patients Rising Now
Preparedness and Treatment Equity Coalition
Support For People With Oral And Head And Neck Cancer, Inc. (SPOHNC)
Triage Cancer

Cancer Support Community Network Partners*

Cancer Support Community at Gilda's Club, Rochester NY
Cancer Support Community Central Ohio
Cancer Support Community Montana
Cancer Support Community Valley/Ventura/Santa Barbara
Gilda's Club Kansas City
Gilda's Club Kentuckiana
Gilda's Club South Florida
Gilda's Club South Florida, Inc.

** Cancer Support Community is a global non-profit network of 190 locations, including CSC and Gilda's Club centers, hospital and clinic partnerships, and satellite locations that deliver more than \$50 million in free support and navigation services to patients and families.*

PATIENTS FOR AFFORDABLE DRUGS NOW™

Comments of

Patients For Affordable Drugs Now to

The Centers For Medicare & Medicaid Services on the

Medicare Drug Price Negotiation Program Guidance

April 13, 2023

Patients For Affordable Drugs Now (P4ADNow) is pleased to offer these comments in support of effective, patient-centered implementation of the [Medicare Drug Price Negotiation Program Guidance](#) provided by the Centers for Medicare & Medicaid Services (CMS) as enacted in the Inflation Reduction Act of 2022.

P4ADNow is the only national patient advocacy organization exclusively focused on lowering prescription drug prices. P4ADNow is independent, bipartisan, and does not accept funding from any organizations that profit from the development or distribution of prescription drugs.

We applaud the timely work by CMS to implement the Medicare negotiation program in accordance with enacted law. According to the [Congressional Budget Office](#) (CBO), this program will benefit the health and financial well-being of patients across the United States – especially those living with acute and chronic illnesses.

We're pleased to offer comments on elements of the guidance that are particularly consequential to patients: transparency, closure of potential loopholes in order to maximize inclusion of as many products as possible, and an easily accessed fair price.

Section 30: Identification of Selected Drugs for Initial Price Applicability Year 2026

We understand CMS issued *Section 30* as final guidance in order to implement negotiation in a timely manner, we want to take the opportunity to commend the agency on the three elements within the section that will benefit patients by closing potential loopholes that could have limited the positive impact of the law on patient and public health. Major pharmaceutical corporations have a well-documented track record of predatory business strategies, anti-competitive tactics, abusive pricing, and market manipulation. For this reason, we applaud CMS for developing guidance that minimizes the opportunity of manufacturers to undermine the Secretary's negotiation authority to the detriment of patients.

Defining Single Source Drugs

P4ADNow welcomes CMS' process, in accordance with statute, for defining a qualifying drug by aggregating across all dosage forms and strengths, thus preventing potential gaming through "product hopping." Likewise, we appreciate that "time elapsed" since approval will be counted from the year of earliest approval among all products with that active ingredient. We are concerned that because a competing product [ANDA or 351(k) BLA] for any dosage or strength of the drug exempts a drug from selection under this section, manufacturers will game the process. Therefore, when determining whether the manufacturer of the competing product is engaging in "bona fide" marketing, we urge CMS to apply a stringent threshold to ensure the competing product has made meaningful market penetration and is easy for patients to access. CMS should issue precise definitions of this threshold to ensure robust competition is occurring and limit unnecessary exclusions from the negotiation process.

Low-Spend Medicare Drug Exclusion from Qualifying Single Source Drugs

P4ADNow commends CMS' approach to excluding "low spend" drugs. Namely, defining drug spending based on gross expenditures instead of net spending will maximize the number of drugs that can be eligible and therefore maximize patient benefit.

Delay in the Selection and Negotiation of Certain Biologics with High Likelihood of Biosimilar Market Entry

P4ADNow appreciates the scrutiny required by CMS in order to grant "delay requests" under this section. Specifically, we applaud the following elements designed to ensure a biosimilar manufacturer seeking the delay is not working on behalf of or in conjunction with a brand-name biologic manufacturer seeking to avoid selection for negotiation:

1. The biosimilar product must be approved *and marketed* within one year of FDA approval.
2. The biosimilar manufacturer cannot be the same as the reference product (branded biologic) manufacturer.
3. The biosimilar and reference product manufacturer cannot have entered into settlements that require or induce the biosimilar to limit market share.
4. The biosimilar manufacturer must demonstrate that patents will not be a barrier to market entry for the competing product.
5. The biosimilar manufacturer must demonstrate it is operationally ready to market the drug in time.

P4ADNow appreciates the stringent processes developed by CMS for carrying out #3, #4, and #5 and encourages the agency to apply equivalent levels of scrutiny to all areas of implementation where proof of competition is required, including the definitions of a qualifying single source drug.

Section 40: Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026

Confidentiality of Proprietary Information

CMS is seeking comments on “the proper balance between the public’s interests in transparency and the protection of business information.” In the case of treatment of proprietary information, we urge that in every instance, CMS defaults to greater transparency, not less.

We are concerned that CMS will treat research and development (R&D) data as proprietary information (except in the cases where prior federal funding is involved). Independent researchers [have found](#) that R&D costs for a new drug range from \$100 million to \$1 billion while pharmaceutical industry-supported studies estimate the cost at more than \$2.87 billion. The widely disparate estimates carry grave implications for drug pricing in the United States. Every product approved by the Food and Drug Administration (FDA) [has](#) some measure of federal support and the Defense Advanced Research Projects Agency (DARPA), the Biomedical Advanced Research and Development Authority (BARDA), and the National Institutes of Health (NIH) play an integral role in the development of many breakthrough drugs. As a result, taxpayers are investors with a substantial interest in identifying an accurate total cost for development of a drug. Orphan drugs [receive](#) additional special benefits, including tax credits for clinical trials, exemptions from user fees, exemptions from 340B discounts, and priority review vouchers. At the minimum — and where legally permitted — CMS should aggregate estimates or publish deidentified data on R&D costs so researchers, policymakers, and advocates can obtain accurate information on drug development costs, free from the bias of pharma-funded research.

While projected market data, revenue, and sales volumes may be proprietary, we urge CMS to provide data publicly on *historic* sales, revenue, and market data. In many cases, such data are public but practically impossible or cumbersome for researchers, policymakers, and advocates to locate and use. *Again, as investors in nearly [every](#) FDA-approved drug, taxpayers are entitled to have access to as much information as legally permissible when considering drug products subject to negotiation in a public insurance program.*

P4ADNow urges CMS to likewise organize and publish data not treated as proprietary, including information on prior federal funding, approved patent applications, exclusivities, and approvals. While much of this data is available to the public in theory, there are numerous barriers to access, including the need for technical expertise, to locate and analyze. The pharmaceutical supply chain contains many complicated inputs, variables, and players, making it indecipherable to a lay person or patient seeking information on their medication. In many cases, the complexity is intentional because it prevents consumers from discovering and revealing information on unjust drug prices. Through its new negotiation authority, CMS can make the playing field slightly

more level by ensuring that data is public and more easily accessible at every possible opportunity.

Section 50: Negotiation Factors

Evidence About Therapeutic Alternatives for the Selected Drug

P4ADNow is pleased that CMS will consider information on therapeutic alternatives submitted by any interested party, including patients, clinicians, and academic experts, as well as real-world evidence. By relying on evidence submitted by entities without a financial stake in the negotiation process, CMS is increasing trust in the negotiation process, since consumers have [well-documented mistrust](#) of research that is sponsored by the manufacturer of a product; and because research sponsored by the drug manufacturer [often results](#) in outcomes [favorable](#) to the sponsor and biased towards its products. We appreciate the agency's factors for scrutinizing evidence, especially the prioritization of peer review, risk of bias, and study population as it compares to Medicare beneficiaries.

Use of Comparative Clinical and Cost Effectiveness Measures

As a patient group, we know that the clinical value of a drug is the most important factor in determining a fair price. One common objection to value analysis as practiced around the world is that it sometimes relies on a measure called the Quality Adjusted Life Year — or QALY. There [is concern](#) in the disability community that “the QALY metric puts a lower value on the life of an individual living with a disability, and, as such, value assessments using this metric devalue treatments for people with disabilities.” P4ADNow supports clear protections against discrimination such as those included in the Inflation Reduction Act that state: “...the Secretary shall not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled or not terminally ill.”

We agree with CMS' approach to the use of QALYs in research when considering therapeutic alternatives and believe it does not discriminate against people with disabilities, the terminally ill, or the elderly. In fact, all of CMS' efforts to “achieve the lowest maximum fair price for each selected drug” will improve the lives of millions of disabled, elderly, and/or chronically ill people in this country whose health is harmed by high drug prices. We encourage the agency's use of explicitly non-discriminatory measures such as the equal value of life years gained (evLYG).

Section 60: Negotiation Process

Methodology for Developing an Initial Offer

In cases of robust generic competition among therapeutic alternatives, P4ADNow supports CMS starting negotiations with an average net price or average sales price (ASP) of those alternatives. But where therapeutic alternatives exist as branded products (or generic or biosimilar products with little to no price competition), we are concerned this approach ties starting prices to prices that are already the [highest](#) in the world. And while net prices are appropriate in cases where the manufacturers of therapeutic alternatives are providing rebates, net prices are not discounted significantly from list prices in cases where a manufacturer offers only small rebates or does not offer rebates, such as cases where there is minimal competition.

In cases where the net price or ASP is greater than the statutory ceiling or where no therapeutic alternative exists, we encourage CMS to use the cost of manufacturing and adjust up or down depending on clinical benefit and Big Four pricing.

Considering Manufacturer Data

We're glad that CMS will be considering R&D cost and the extent of federal financial support for the selected drug product during negotiations in accordance with statute. We implore CMS to use the broadest possible definitions for "preclinical" and "novel discovery" in order to capture taxpayer-funded grants that occur far before a manufacturer acquires a viable drug product.

Publication of the Maximum Fair Price (MFP)

Section 60.6 details CMS' intention to post on the CMS website the name of the selected drug, the initial price application year and an annually updated "MFP file" showing the inflation-adjusted price for the drug. P4ADNow applauds the transparency and accessibility of this intended practice and urges CMS to explore the most effective ways in which to ensure that this data are presented in an accessible way so that consumers can best understand the information. We also suggest a webpage intended for consumers that should display at minimum: (1) Brand and generic names for the drug; (2) Price equivalent for all dosage forms; (3) Date the price is in effect; (4) Method for accessing the price and process if MFP is not honored.

Section 70: Removal from the Selected Drug List Before or During Negotiation, or After an MFP is in Effect

Section 70 details the process through which a drug selected for negotiation is removed from the list of selected drugs when it is no longer subject to the negotiation process. P4ADNow is concerned that a selected drug will not be replaced on the list when a competitor to the drug comes to market. If permitted by statute, we encourage CMS to institute a practice in which it replaces each drug removed from the list in a timely manner with another selected drug. This practice would minimize the ability of manufacturers to game this loophole and enhance the opportunity for negotiated prices to benefit patients.

Section 90: Manufacturer Compliance and Oversight

Making MFP Available to Patients

In order to maximize the benefit of the drug price negotiation program, it is critical that the maximum fair price (MFP) is made available to patients effectively and transparently. We want to emphasize the importance of CMS' attention to ensuring that beneficiaries are aware that they deserve access to a specific MFP and that CMS puts in place a straightforward process for patient reimbursement in the event they are charged more than the MFP. We encourage CMS to create materials to educate patients on MFP and to proactively notify patients taking selected drugs when they can expect the lower price and, if overcharged, when and how they might expect to be reimbursed.

Patients who are prescribed a negotiated drug will be at the mercy of the dispensing entity (local pharmacy or mail order pharmacy) to make sure they can obtain the correct price. For this reason, we urge facility, transparency, and a clearly articulated process for pharmacies of all types. CMS presented two equal methods for primary manufacturers to ensure MFP is provided to patients — one prior to the point of sale and one after the point of sale. Providing an option of retroactive reimbursement to the dispensing entity could be administratively burdensome or costly to pharmacies, especially small, independent pharmacies. We are concerned that this difficulty may inadvertently result in patients not being able to access the fair price at the point of sale due to uncertainty about MFP. Instead of offering a proactive and retrospective process to manufacturers as equal options, we urge CMS to incentivize use of the MFP at the point of acquisition by the pharmacy. The agency could, in the event a manufacturer opts for retroactive reimbursement, require the manufacturer to offer written explanation to the agency for why that option was used.

Access to the MFP at the point of sale is critical to patients who are already burdened by paying excessive prices for drugs while managing illness. Uncertainty at the pharmacy counter or processes that require additional paperwork, inconvenience, or onerous self-advocacy will greatly harm the positive impact of negotiated prices for patients. Wherever possible, it should be the duty and responsibility of CMS to remove unnecessary administrative barriers to access for patients.

Section 100: Civil Monetary Penalties

P4ADNow appreciates the extent to which CMS has gone to craft a process for levying civil monetary penalties for manufacturers that attempt to hide or falsify information in order to maximize compliance with the law and enforce penalties for non-adherence. The strong financial consequences will help to ensure that manufacturers cannot hide pertinent information and will

maximize the likelihood that patients actually have access to the fair price at the pharmacy counter.

Section 110: Part D Formulary Inclusion of Selected Drugs

P4ADNow agrees that formulary inclusion is critical, especially as opponents of Medicare negotiation disparage the law by claiming patients will lose access to needed medications. As a patient group, P4ADNow understands that implementation of this provision is designed to preserve access to all beneficiaries. Furthermore, mandatory formulary inclusion counters the drug industry's arguments that the Inflation Reduction Act will cause disastrous results to the industry's financial viability.

The Medicare program is the largest purchaser of prescription drugs and pays the highest prices in the world. While negotiation will meaningfully lower prices for patients on selected drugs, the government will still pay some of the highest prices in the world for *all* non-selected Medicare covered products, which total [more than 3,500 drugs](#). Required formulary inclusion guarantees the manufacturers of selected drugs access to a market of [nearly 50 million individuals](#), thus countering the industry claim that the law threatens manufacturers' pipelines and patient access.

Conclusion

We appreciate the opportunity to offer comments that emphasize the patient perspective. We urge CMS to prioritize the following elements that are most consequential to patients:

- **Patient-centered:** A comprehensive and fair negotiation process does not help patients unless they are able to obtain the negotiated price at the pharmacy counter. In every instance, we encourage CMS to engage in proactive beneficiary education and consumer-focused processes.
- **Transparency:** Taxpayers play a pivotal role in research behind every drug approved by the FDA and the negotiation process ultimately determines the price paid by taxpayer funds. For this reason, we urge CMS to opt for transparency in every instance, especially relating to R&D costs and other manufacturer-provided data.
- **Accountability:** Recent congressional [investigations](#) have demonstrated that the pharmaceutical industry engages in unscrupulous tactics that undermine the law, artificially prolong monopolies, and harm patients. Big drug companies have not earned the benefit of the doubt, so we urge CMS to continue to implement the negotiation process under the assumption that pharmaceutical companies will exploit loopholes wherever possible.



The Honorable Meena Seshamani, M.D., Ph.D.
Deputy Administrator and Director
The Center for Medicare
7500 Security Blvd
Baltimore, MD 21244

RE: Medicare Drug Price Negotiation Program Guidance Memo

Dear Dr. Seshamani,

On behalf of Patients Rising Now, thank you for allowing comments regarding the Centers for Medicare and Medicaid Services' (CMS) implementation of the Medicare Drug Price Negotiation Program provisions of the Inflation Reduction Act (IRA). Congress failed to make this law patient-centered, but CMS can still place the voice of the seniors the Agency serves first in drug pricing decisions and the law's implementation.

Formed in 2015, Patients Rising Now has developed a significant following of over 110,000 patients and caregivers and has guided them on their journeys to advocate for themselves and their loved ones to get the care and treatments they need to live a fulfilling life. As a patient advocacy organization, PRN supports reforms and legislation aimed at advancing patient access to affordable, quality healthcare.

While nothing in the Inflation Reduction Act requires a patient-centered approach, it is important that CMS understand that it is the patient that has the best understanding of what constitutes value when assessing a medicine. It is critical for seniors that CMS not follow the flawed model of organizations like the Institute for Clinical and Economic Review (ICER), which simulate cost-effectiveness from the payer's perspective. Patients frequently experience benefits from a therapy that are not captured by the health system. ICER's generalized, unscientific, and assumption-based models do not capture patient experience with any individual treatment. Patient engagement should be at the core of the IRA implementation and any decision on drug pricing. Relying on a small cadre of health economists, academics, and bureaucrats will create a narrow perspective that is evident in the initial guidance memo from CMS. How CMS is considering drugs based on unmet medical need is far too limited and unsophisticated.

Per the initial guidance memo, CMS "...intends to define [unmet medical need] as treating a disease or condition in cases where very limited or no other treatment options exist." This definition, as written, is shortsighted and increases the probability for misapplication or politicization of the term unmet medical need for diseases and their respective treatments in the future. This goes beyond a matter of semantics. A definition such as this will inform CMS' decisions on and interpretation of the IRA in the years to come. To that end, it is important that CMS amends this definition to be more in line with existing definitions of unmet medical need, not the least of which being the definition in the IRA: the very law that this guidance memo is seeking to implement.

PATIENTS RISING NOW

The FDA, as part of its Guidance for Industry on Expedited Programs for Serious Conditions – Drugs and Biologics (section III, subsection C), defines unmet medical as “...a condition whose treatment or diagnosis is not addressed adequately by available therapy.” This definition is far more comprehensive, more accurately reflects the healthcare landscape for many rare & chronic disease patients, and it creates more potential for better treatments to find their way to the patients who need them most. The definition of unmet medical need, as stated in the IRA, is nearly identical to the FDA definition, so any Agency action on this law must be more in keeping with the bill text.

In the guidance memo, we are pleased to see that the quality-adjusted life year (QALY) will not be used in the negotiation process. However, that is the extent of the prohibition. It does not extend to other areas of CMS such as Medicaid and the Children’s Health Insurance Program, both of which have been known to utilize the QALY in coverage and reimbursement decisions. The QALY is highly subjective and notorious because it discounts the lives of the elderly, the disabled and others who cannot achieve maximum QALY scores - and, thus, will never achieve the highest “quality of life. Given that the QALY is inherently discriminatory against rare disease patients, chronic disease patients, disabled patients, and seniors, its use in Federal and State health programs should be prohibited across the board. While it is encouraging that the new Negotiation Program will not allow QALYs, Patients Rising Now would like to see a similar ban for the rest of the Agency’s activities.

Solicitation of public comments on matters such as these are a critical aspect of Agency function and ensure any actions taken aren’t in direct contrast with the public and relevant stakeholders. In this guidance memo, CMS expresses the intention to solicit public comments on numerous facets of this complex law. However, in reference to section 30 of this memo (the implementation of the Negotiation Program for years 2026, 2027, and 2028), CMS not only declines to permit the customary notice-and-comment period but cites it as “...impractical, unnecessary, and contrary to the public interest.”

We understand that Congress did not craft the IRA as a patient-centric law, but excluding patient engagement is wrong. The drug price negotiation provisions of the IRA are unquestionably the most important part of the IRA and represent the most sweeping changes to Medicare since the implementation of Part D. Unilateral measures such as this are troubling to say the least and do not bode well for Agency implementation of Congressionally passed legislation in the future.

To that end, CMS must adopt a patients-first culture, where all decisions begin and end with their interest in mind. It is imperative that CMS develop clear, transparent processes for making decisions that are patient-centered and promote collaboration with patients in the decision-making processes. CMS must support the use of value-based coverage recommendations driven by the clinical value of the treatments, patient input, and real-world evidence. How patient experience and related data are quantitatively applied in the determination of a drug’s value and price in Medicare should always be publicly disclosed.

PATIENTS RISING **NOW**

Thank you again for holding a comment period on implementation of the IRA. These recommendations and others would not be possible without dedicated and frequent comment periods. Solicitation of comments from the public and relevant stakeholders is key to Agency making sound and informed decisions. And it is of the utmost importance that it continues so no missteps or unintended consequences occur as key provisions of this law take effect.

Sincerely,

A handwritten signature in black ink that reads "Rachel Derby". The script is fluid and cursive, with the first letters of each word being capitalized and prominent.

Rachel Derby
Executive Director



April 14, 2023

Meena Seshamani, M.D., Ph.D.
Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-1850
Attn: PO Box 8016

Sent electronically to IRAREbateandNegotiation@cms.hhs.gov

**Re: Medicare Drug Price Negotiation Program: Initial Memorandum,
Implementation of Sections 1191 – 1198 of the Social Security Act for Initial
Price Applicability Year 2026, and Solicitation of Comments**

Dear Deputy Administrator Seshamani:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising more than 220 institutions from across the health care spectrum, thanks the Centers for Medicare & Medicaid Services (CMS) for the opportunity to submit comments on the *Medicare Drug Price Negotiation Program Initial Guidance* for the initial price applicability year (IPAY) of 2026.¹ CMS' implementation of the drug price negotiation program established by the *Inflation Reduction Act (IRA)* represents an unprecedented new federal authority that will significantly alter how personalized medicine will be evaluated and incentivized under Medicare. We believe the initial guidance lacks clear descriptions for CMS procedures and methodology that will be used to negotiate a drug's maximum fair price (MFP). Because few details are provided on how personalized medicine will be considered, we are concerned about how CMS' implementation of the new program may impact patient access to new and existing treatments underpinning this approach to care.

Personalized medicine is an evolving field in which physicians use diagnostic tests to determine which medical treatments will work best for each patient or use medical interventions to alter molecular mechanisms that impact health. By combining data from diagnostic tests with an individual's medical history, circumstances, and values, health care providers can develop targeted treatment and prevention plans with their patients. Personalized medicine is playing an important role in transforming care and patient outcomes for a range of serious and life-threatening diseases and conditions, helping to shift patient and provider experiences away from trial-and-error toward a more streamlined process for making clinical decisions.

After initial approval of a targeted therapy by the U.S. Food and Drug Administration (FDA), further research provides greater understanding of patients' responses to treatment based on results from molecular diagnostics and other biomarkers. This

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research leads to new or improved treatment indications that contribute to progress in personalized medicine. Of particular importance is the role that research conducted after approval of a new drug plays in advancing the frontiers of personalized medicine and the potential downstream impacts of the negotiation program on this research.

We believe PMC and CMS share the goal of achieving better health outcomes and lowering costs for patients. The following comments express concerns over how the drug price negotiation program could disrupt the innovation ecosystem for and patient access to personalized medicine. As overarching priorities, PMC urges CMS to refine its negotiation process to ensure:

- CMS' methodology to determine a selected drug's MFP recognizes the clinical and societal benefits of personalized medicine and incorporates patients' perspectives on care value;
- CMS' methodology and negotiation process establish consistency and transparency by communicating how factors considered are weighed and how external data is factored into its decisions;
- CMS establishes procedures that allow a robust exchange of information with manufacturers, patient organizations, and other stakeholders in determining the MFP throughout the negotiation process, as well as procedures that allow information about negotiations to be shared publicly to help establish precedents and consistency across negotiations;
- Patients do not face additional barriers in accessing negotiated medicines and their treatment alternatives, as well as non-negotiated medicines; and
- CMS establishes processes to monitor any unintended, downstream impacts of the program on patient access to personalized medicine and on pipelines for new personalized medicine treatments and expanded indications.

Statement of Neutrality

Many of PMC's members will present their own responses to the *Medicare Drug Price Negotiation Program Initial Guidance* and will actively advocate for those positions. PMC's comments are designed to provide feedback so that the general concept of personalized medicine can advance, and are not intended to impact adversely the ability of individual PMC members, alone or in combination, to pursue separate comments with respect to the initial guidance and/or any that follows.

Recognizing the Clinical and Societal Value of Personalized Medicine

Drugs with personalized medicine treatment strategies create considerable benefits for patients and society since they are used in a manner that directs them toward patients who are most likely to benefit and away from those who are not. Value assessment frameworks (VAFs) often draw sweeping conclusions, however, about the economic worth of a particular treatment, typically based on analysis of its safety and effectiveness at a population level. In many cases, value assessment methodologies fail to adequately account for the safety and effectiveness benefits that may be realized by individual patients or patient subpopulations. When assessing value, it is important to consider the holistic benefits of a treatment at the patient, subpopulation, and societal levels.

PMC appreciates CMS' reference to patient experiences in its discussion of the clinical benefits of selected drugs and their therapeutic alternatives in Sec 60.3.3. However, as we discuss later in this letter, it is still unclear how patients, caregivers, and providers will influence the selection of therapeutic

alternatives or if CMS will seek guidance throughout the MFP-setting process from these key stakeholders. Considering patient experiences in this context is paramount to ensure that patient perspectives of value are appropriately accounted for during the drug price negotiation process. In 2017, PMC published a white paper titled [*Personalized Medicine and Value Assessment Frameworks: Context, Considerations, and Next Steps*](#).ⁱⁱ The paper outlines factors that value assessment frameworks should consider to help ensure a focus on patient experiences and patient access to optimal care. **In general, PMC urges CMS to consider the following aspects of clinical and societal value related to personalized medicine that advance patient-centered care, ensuring that the value of personalized medicine to direct patients toward or away from treatments based on their likelihood to benefit from them is factored into determining the MFP for a selected drug:**

- 1. Diagnostic testing strategies:** Diagnostic tests can help guide treatment decisions and determine which treatments will be most effective and safest to use in any given patient and are a crucial element of the personalized treatment regimen. For example, the use of companion diagnostics can help define subpopulations of patients who may benefit from a treatment, and those that will not. The availability of diagnostic tests and consideration of test results that help inform treatment decision-making for drugs with biomarker implications must be figured into the value assessment methodology for personalized medicines. **PMC encourages CMS to consider the value of applicable diagnostic strategies in its evaluation of unmet medical need and clinical effectiveness.**
- 2. Heterogeneity of treatment effects:** Some patients will experience more or less benefit from a treatment than suggested by the averages reported within clinical trials and population-based data. Health care policies based on average, population-based rates for treatment response may unduly restrict access to treatments that could be the most effective option for some patients. Thus, personalized medicines may be misjudged or undervalued simply because the data required for value-based decision-making do not account for patient subpopulations or because long-term efficacy data is not yet available. **PMC encourages CMS to consider the full range of patient outcomes and benefits that may not be represented in population average-based data.**
- 3. Patient values and circumstances:** Personalized medicine depends not only on the consideration of a patient's molecular characteristics and biological characteristics but also on individual values, clinical and economic circumstances, and the potential impact of a therapy for that patient over the long term. Fundamental patient values and preferences, including the impact of treatment on quality of life, quantity vs. quality of time, functional ability related to illness or treatments, cost of supportive care, and other patient costs of treatment are weighed by patients and their caregivers when deciding on a treatment in consultation with health care providers. **To appropriately assess the value personalized medicines provide to patients with unmet medical needs, PMC encourages CMS to not use the narrow definition of "unmet medical need" proposed in guidance and instead formally consider a broad range of patient outcomes and impacts, including unmet medical needs unique to individual patients and to patient subpopulations.**
- 4. Treatment efficiency:** Although value assessments generally focus on improvements in effectiveness, they do not generally consider treatment efficiency. Treatment efficiency involves avoiding ineffective or harmful treatment options and reducing the downstream expenses

associated with rapid disease progression and/or adverse events. In order to capture economic as well as clinical value, value assessments need to consider costs and outcomes across health care. **As CMS evaluates the costs and benefits of personalized medicines to society, PMC encourages the agency to formally consider a broad range of economic impacts, including broader cost offsets and societal benefits.**

As discussed in the following section, we recommend that when these factors are taken into consideration, the MFP for a selected drug, including any selected personalized medicines or targeted therapies, be set at the ceiling if it demonstrates significant clinical and societal benefit.

It is clear both in the statute and in CMS' initial guidance that quality-adjusted life years (QALYs) will not be used as a basis for evaluations. The QALY does not sufficiently account for the broad heterogeneity of clinically relevant characteristics and preferences across patients and diseases, nor does it consider aspects of value defined by patients and their families. The measure relies on population averages that do not consider the heterogeneity of patient populations, even within the same condition.

While CMS states it will follow statute, the guidance indicates that CMS still plans to separate and exclude QALY metrics from evaluations of research that otherwise factor in QALYs. PMC is concerned that this approach may not effectively separate QALYs from CMS' analysis because CMS may continue to rely on studies that employ QALY-related data from secondary sources, or that CMS may exclude analyses that are otherwise helpful in establishing the value of a drug for a patient. **Therefore, PMC requests that CMS make clear how it will exclude QALY-based metrics from its analysis of such evidence, when this evidence may be used, and how this evidence would be weighed. PMC also requests that CMS highlight when and how the agency removed QALY-based metrics from consideration in its public explanation of a drug's MFP. In addition, regarding CMS' *Negotiation Data Elements Information Collection Request* that asks the public to submit information on a selected drug, PMC asks CMS to make sure that data submitters attest to removing the QALY and other potentially discriminatory metrics from their submission, instead of using the proposed checkbox.**

CMS requests input on what alternative measures to QALYs might be appropriate or inappropriate. PMC believes the agency would be better served by focusing on the factors related to comparative clinical outcomes and unmet need that are described in statute, which can better capture the benefits of personalized medicine, rather than seeking an alternative to the QALY. There is not one measure of value or one VAF that holistically captures the value of a treatment and the benefits of any medical treatment including personalized medicine. VAFs have strengths and limitations relative to different stakeholder perspectives and circumstances that can bolster or undermine their usefulness and applicability to personalizing patient care. A single measure will not be sufficiently comprehensive. **We encourage CMS to consider a wide variety of measures consistent with CMS' statutory focus on comparative effectiveness research and unmet need, especially those driven by patient experience data, patient input, and patient-centeredness.**

Establishing a Consistent and Transparent Process for Gathering and Evaluating Evidence

PMC appreciates that CMS will consider real-world evidence (RWE), evidence from peer-reviewed research, white papers, expert reports, clinician expertise, patient experiences, intermediate outcomes, surrogate endpoints, and patient-reported outcomes when reviewing the clinical benefit of a selected drug

and its therapeutic alternatives (Sec. 60.3.3). Considering that all medicines for which CMS will set an MFP have a minimum of seven years since their original FDA approval, **PMC encourages CMS to consider as broad an array of evidence sources and outcomes as possible to help fill gaps in population-based data sources and capture the full range of benefits and impacts from personalized medicine discussed above.**

Although CMS' initial guidance lists aspects related to the quality and completeness of evidence sources it will consider, such as peer review, study limitations, risk of bias, and study population, among others, CMS does not describe requirements for the quality and completeness of this data, nor how CMS would consistently evaluate this evidence in determining the MFP. For example, since studies using RWE are designed fit-for-purpose, CMS' methodology should consider the extent to which the evidence it considers was designed to answer the value questions it is asking. The approach outlined in the initial guidance is too vague to create consistency across negotiations. **To ensure that the agency is evaluating these elements in a way that considers the value of personalized medicine to patients, CMS should refine its methodology through notice and comment rule-making to provide more clarity on how the agency intends to leverage negotiation data elements outlined in Sec. 50.2.** For RWE in particular, CMS should describe what data sources they plan to use and create guidelines to ensure that the data used is robust and correctly utilized.

Specifically, CMS should outline a consistent methodology for how it will synthesize evidence and for how data related to therapeutic alternatives will result in changes to an initial offer or final negotiated MFP. In addition, CMS should leverage clinicians' and patients' expertise and not use cost as a criterion for selecting therapeutic alternatives. While multi-criterion decision analysis (MCDA) may not be feasible for CMS because it requires extensive time, resources, and expertise, CMS may be able to incorporate elements from, for example, the cost-consequence approach model to compare evidence on outcomes for certain therapies. As part of CMS' methodology, we ask CMS to prioritize data related to the factors described above for recognizing the full range of personalized medicine's benefits to patients and the health care system. Given the discount already reflected in a selected drug's ceiling price, **we recommend that when these factors are taken into consideration, the MFP for a selected drug be set at the ceiling if it demonstrates significant patient benefit.**

Furthermore, CMS' methodology should clearly explain how each data element is weighted in determining the initial offer and final MFP. **To account for the clinical and societal benefits of personalized medicine and incentivize continued research and development for this field, CMS should place more weight on the factors related to the benefits of the selected drug for patients, caregivers, and society over, for example, non-clinical manufacturer-specific data elements.**

Establishing a consistent process for gathering and evaluating evidence can help manufacturers, patient groups, and other third parties better understand the evidence they may need to discount, prioritize, or collect for CMS' future consideration. Transparency can also build beneficiaries' confidence that their preferences and values are important to the agency.

Facilitating Meaningful Stakeholder Engagement

We recognize that CMS has a tight timeline for drug selection and price negotiation. But in order to ensure MFPs adequately reflect the value of selected treatments for patients and to limit unintended consequences on patients' access to personalized medicine, CMS must provide ample time for third

parties, including patients and patient organizations, to share data and experiences related to selected drugs.

CMS' initial guidance only allows 30 days from when the list of selected drugs is announced for the public to provide information on the selected drug and therapeutic alternatives to inform CMS' initial offer. We believe this short and singular timeframe for public input does not allow a sufficient window for stakeholders who may have information on the value of a treatment to their patient population to collect and provide information that could improve CMS' decision-making. In addition, this timeframe will disadvantage patients and caregivers from or organizations working with underserved communities who have fewer resources and may find it challenging to respond in such a short timeframe. **CMS should consider the burden of data collection and submission on stakeholders. We ask CMS to allow patients, caregivers, clinicians, and organizations representing these groups additional time to submit the requested data after the list of selected drugs is published. In addition to informing CMS' initial offer for a selected drug, CMS should allow this information to be submitted during subsequent steps of the negotiation process, if initiated, to inform CMS' decision-making.**

Flexibility with the submission of public information would facilitate the inclusion of a broad range of patient perspectives, including those of communities underrepresented in existing studies and published literature.

Noticeably, the proposed negotiation process does not allow for additional engagement with third parties beyond the initial 30-day window to submit data. CMS' final public explanation of the MFP is released six months after the only opportunity for public input. This does not build confidence that patient and stakeholder input will be reflected in the final MFP. **Patients, caregivers, providers, manufacturers, and regulators should all be engaged meaningfully throughout the negotiation process. These parties should be allowed ample opportunities to submit relevant information. And they should be informed by CMS about how their input is being used during the negotiation process.** In addition, although we appreciate CMS' intention to consult with clinical and academic experts to help evaluate clinical benefit of a selected drug, **we ask CMS to outline how clinical and academic experts would be identified and consulted during the negotiation process.** For example, CMS could establish a panel of patients, clinicians, and other stakeholders to provide feedback throughout each drug negotiation.

We appreciate CMS' request for input on striking the proper balance between the public's interests in transparency and the protection of confidential business information. CMS' initial guidance proposes that any information the manufacturer receives from CMS about the initial offer and negotiation factors during the negotiation process must be kept confidential and must later be destroyed (Sec. 40.2). Although we agree CMS needs to preserve the confidentiality of a manufacturer's proprietary information, the confidentiality and compliance requirements around the information manufacturers receive from CMS creates an opaque negotiation process. These requirements would prevent setting precedents and sharing lessons learned across negotiations, potentially undermining manufacturers' and the public's confidence in the consistency of negotiations and the determination of MFPs across selected drugs. **We ask CMS to allow manufacturers to publicize information related to the negotiation while still protecting private trade information.** This will not only help build public trust in the process, but will ensure transparency and predictability that will help inform stakeholder data submissions during future years of the negotiation program.

In order to improve their ability to participate in the negotiation process, stakeholders must understand how the information they submit was considered. We thank CMS for intending to publish an explanation

of the factors that had the greatest influence in determining a drug's MFP (Sec. 60.6.1). We are concerned, however, that the explanation may not provide adequate detail to be meaningful to the public and that its timing, six months after the initial opportunity for public input, may make it irrelevant for stakeholders. **In CMS' explanation for the MFP, we ask the agency to explain which information submitted by the manufacturer and the public was or was not considered in the final MFP; the benefits and impacts considered; the data sources considered; how evidence influenced the MFP up or down, including the extent to which RWE and patient-centered data elements like patient experience data were used; which third parties were engaged, both formally and informally by CMS; and, as discussed above, the extent to which and how any evidence used to inform the MFP was separated from a QALY-based metric. In addition, we recommend CMS make explanations for the MFP clear, accessible, and transparently available for the public.**

Ensuring Coverage Policies Facilitate Patient Access to Negotiated Drugs

PMC requests CMS clarify how it will interpret the requirements identified in Sec. 110 that negotiated drugs be covered by plans, specifically the extent to which any utilization management will be permitted for negotiated drugs. PMC has previously submitted comments to CMS on the difficulties utilization management practices, such as prior authorization and step therapy, can create for patients in accessing the latest treatments and standards of care informed by personalized medicine.^{iii,iv} Without additional clarification and guardrails, PMC is concerned that plans could use utilization management to prefer non-negotiated drugs or deny coverage for negotiated products vital to a patient's personalized health care. Because negotiated drugs are being offered to plans at a lower price, **PMC believes negotiated drugs should not face additional cost-control practices that could limit eligible Medicare beneficiaries' access to them. To ensure patients are protected from plan attempts to offset costs, CMS should establish robust guardrails and conduct oversight to ensure the clinical appropriateness of any utilization management and formulary changes and to mitigate unintended consequences on beneficiaries' access to both negotiated and non-negotiated drugs and the narrowing of patients' treatment options.**

Monitoring Unintended Impacts on Personalized Medicine

Now an important part of health care, personalized medicines have accounted for at least a quarter of new drug approvals for each of the past eight years.^v Over the past eight years, PMC has also identified more than 120 expanded indications significant to advancing personalized medicine.

Multiple analyses, including those from the Congressional Budget Office, have called attention to the potential consequences of the Medicare drug price negotiation program, such as canceled research and development and disincentives to invest in small molecule medicines and therapeutic areas that require incremental innovation.^{vi,vii,viii,ix} Due to smaller patient subpopulations, personalized medicines that address the root causes of disease can be expensive and riskier to develop. In 2022, over half of FDA-approved personalized medicines were indicated for certain cancers, and over one-third were indicated for rare diseases.^x Treatment pipelines in both therapeutic areas are expected to be impacted by Medicare's drug price negotiation program.^{xi,xii} In addition, over the past eight years, the expanded indications listed in PMC's annual analyses of FDA approvals have had an upward trend in the average time since a drug's initial approval. Given this trend, PMC is concerned that implementation of the negotiation program, which by statute makes drug products eligible for negotiation after seven years (or

11 years for biological products), could curtail post-approval research for expanded indications that provide patients with personalized medicine treatment options.

Since Medicare's drug price negotiation program could have an outsized effect in discouraging the pharmaceutical industry from bringing additional personalized medicines and expanded indications to the market, CMS should take every step possible to prevent and monitor for potential unintended impacts of the program on patients and the health care system. **PMC asks CMS to collect information on unintended impacts to ensure the negotiation program does not create disincentives to develop new treatments for unmet medical needs; disincentives to conduct research on expanded indications that provide additional benefits to patients; or barriers for patient access to personalized medicine.** Related data CMS could consider tracking include changes in new drug applications (NDAs) and supplemental NDAs; changes in formulary placement and utilization management for negotiated versus non-negotiated drugs; and other barriers to patient access.

Conclusion

PMC appreciates CMS' commitment to lowering health care costs for Medicare beneficiaries. As the agency implements the drug price negotiation program, we urge CMS to carefully consider these comments for this and future guidance. We look forward to working with you and your colleagues to ensure the program maintains the ecosystem for innovation in personalized medicine and fosters patient access to needed personalized medicine treatments. If you have any questions about the content of this letter, please contact me at 202-499-0986 or cbens@personalizedmedicinecoalition.org, or David Davenport, PMC's Manager of Public and Science Policy, at ddavenport@personalizedmedicinecoalition.org or 804-291-8572.

Sincerely yours,



Cynthia A. Bens
Senior Vice President, Public Policy

ⁱ Center for Medicare. *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments*. March 15, 2023. <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>. (accessed April 13, 2023).

ⁱⁱ Personalized Medicine Coalition. *Personalized Medicine and Value Assessment Frameworks: Context, Considerations, and Next Steps*. December 14, 2017. https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_and_VAFs.pdf. (accessed April 13, 2023).

ⁱⁱⁱ Personalized Medicine Coalition. *Comment letter on Medicare Program; Request for Information on Medicare (CMS-4203-NC)*. August 31, 2022. <https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PMC-Comment-Letter-on-Medicare-Advantage-RFI.pdf>. (accessed April 13, 2023).

^{iv} Personalized Medicine Coalition. *Comment Letter on Step Therapy for Part B Drugs in Medicare Advantage (MA)*. October 15, 2018. https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PMC_Comment_Letter_Step_Therapy.pdf. (accessed April 13, 2023).

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April 14, 2023

VIA Electronic Filing – IRAREbateandNegotiation@cms.hhs.gov

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Re: Medicare Drug Price Negotiation Program: Draft Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Deputy Administrator Seshamani:

Pfizer Inc. appreciates the opportunity to submit comments on the Centers for Medicare and Medicaid Services' (CMS) *Medicare Drug Price Negotiation Program: Draft Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026*¹ (henceforth referred to as the “Guidance”). Pfizer Inc. is a research-based, global biopharmaceutical company. We apply science and our global resources to bring therapies to people that extend and significantly improve their lives through the discovery, development and manufacture of medicines and vaccines.

The Inflation Reduction Act established the so-called “Medicare Drug Price Negotiation Program”, which in fact, is not a true “negotiation” framework, but a dangerous price setting policy that will significantly harm patient access to medicines and threaten U.S. leadership in biopharmaceutical research and development. These threats are inherent to the law, which requires the Secretary of Health and Human Services (HHS) to disrupt the very real negotiations between manufacturers and Part D plans by setting the price for any top spend small molecule drug that has been on the market 9 years or more without generic competition and any top spend biologic that has been on the market for 13 years or more without biosimilar competition. As such, the law requires HHS to intervene in private market negotiations well before most products have reached the end of their patent and other legally provided exclusivity periods. This ill-conceived policy is already leading to shifts in biopharmaceutical investment and is likely to impact the pace of innovation in the U.S.

We refer to this new program as government price setting rather than a true “negotiation” because manufacturers who do not enter into the process are subject to per-day excise taxes starting at almost twice the sales of the selected drug and increasing to 1,900 percent of a drug’s total revenues. Further, the only way to avoid those excise taxes would require that a manufacturer terminate coverage in Medicaid and Medicare Parts B and D for all the manufacturer’s products – not just the selected product – when almost half of annual nationwide spending on prescription medicines is through Medicare and Medicaid.

¹ In addition to the comments included here, Pfizer fully supports the additional, comprehensive comments submitted by the Pharmaceutical Research and Manufacturers of America (PhRMA).

We know what happens when governments set prices for medicines – investment and innovation in biopharmaceutical research diminishes and people in those countries have less access to vital medications that could save their lives. For example, to the extent that patients in other developed countries with price controls on drugs have access to medicines, they have to wait longer to access those medicines compared to patients in the United States (e.g., 3 months on average in US vs. 20 months in Australia, 18 months in France, 16 months in Japan, 15 months in Canada, and 11 months in the UK).² In addition, recent research has found that 60% of FDA approved medicines from 2011- 2020 originated in the United States. The FDA approved 363 new medicines over that time period, and the US was solely responsible for the origination of 223 of those medicines.³ There is robust evidence that America’s free market approach to drug development and pricing fosters leadership in the global biopharmaceutical industry and simultaneously encourages broad and timely access to new and existing innovations in pharmacologic treatments.

As CMS is implementing this law, the agency has the opportunity to mitigate some of the negative consequences that can result when governments set prices for medicines through thoughtful, detailed, and careful rulemaking and guidance. However, we are concerned that the policies outlined in the Guidance instead will impose requirements difficult for manufacturers and other stakeholders to fulfill, exacerbate manufacturer burdens, and most important, threaten the ability of manufacturers to develop the best innovations in pharmacological treatments that save improve lives in the U.S. and around the world.

In addition to inherent flaws associated with price setting, CMS’ Guidance is laden with misconceptions, burdensome requirements, and a significant lack of clarity. The flaws in the Guidance do not simply burden Pfizer and other manufacturers, but instead place biopharmaceutical manufacturers in an impossible position, caught in tight timeframes, buried in mounds of paperwork to piece together ultimately unattainable data, and narrowly focused on government price reporting instead of innovations for patients.

Pfizer hopes to partner with CMS to lend our firsthand experience and deep understanding of the US biopharmaceutical industry to develop a thoughtful approach to implementation of the drug price setting program in a way that mitigates harm to American leadership in drug discovery and development and to American patients. Pfizer is deeply troubled by the Guidance and how it will exacerbate the effects of a flawed policy. The value of American biopharmaceutical innovation is felt by millions of Americans, as evidenced by the dramatic progress we were able to make against the COVID-19 pandemic in recent years. Thanks to decades of investment in mRNA technology, Pfizer and other companies were able to quickly bring innovative vaccines and treatments to market that transformed the trajectory of the pandemic. The new approach to price setting in Medicare threatens the pace and impact of innovations like these. Accordingly, we strongly urge CMS to revise its Guidance to lessen these risks. While our comments on each section of the Guidance are provided in more detail later in this letter, we highlight a few key issues here:

- **The Guidance confirms concerns that CMS will have unfettered power to set prices based on subjective judgements.**
 - The lack of specificity in how CMS will define and weigh the individual manufacturer and product specific “factors” about selected drugs, combined with opaque procedures, results in a price setting process that will appear subjective and arbitrary in direct violation of the legal requirement for a clear and reasonable framework. We urge CMS to

² PhRMA analysis of IQVIA Analytics Link. June 2020; PhRMA analysis of Food and Drug Administration (FDA), European Medicines Agency (EMA), Pharmaceuticals and Medical Devices Agency (PMDA), Health Canada, and Therapeutic Goods Administration (TGA) data. June 2020.

³ [The US Ecosystem for Medicines: How new drug innovations get to patients Government, Academia, Small firms, and Large firms, 2011 – 2020](#). Vital Transformations. March 2023

make changes to provide needed clarity and specificity in the price-setting methodology and factor definition.

- CMS' starting point for the initial offer amounts to therapeutic reference pricing and gives CMS the ability to make judgments about clinical similarity without sufficient opportunities for stakeholder input.
 - We are concerned this will result in prices that don't reflect the value these medicines bring to patients and society, and thus Pfizer recommends that CMS undertake a scoping process and engage with manufacturers prior to determining an initial offer.
- **The Guidance creates legal obligations on companies that may be impossible to meet.**
 - CMS proposes to establish separate categories of "primary" and "secondary" manufacturers, and to hold primary manufacturers responsible for other distinct corporate entities. Primary manufacturers of a selected drug would be required, among other things, to collect and submit data from any secondary manufacturer, ensure that any secondary manufacturer make the government-set price available, and pay any civil monetary penalties for violations (including those stemming from noncompliance by any secondary manufacturer). This proposal is impractical and opens any manufacturer engaging in the price-setting process with CMS to myriad procedural and legal difficulties. Pfizer urges CMS to negotiate separate Agreements with any distinct manufacturer.
 - CMS proposes to require primary manufacturers to provide access to the MFP and describes of two options that are not viable without the necessary supporting supply chain infrastructure and data reporting necessary for manufacturers to verify claims eligibility. In particular, we urge CMS to designate a third-party administrator (TPA) to facilitate this process for manufacturers.
 - Attributing R&D costs to a particular drug or combination of drugs presents a significant challenge. Manufacturers and investors typically invest in research & development for "programs" in a specific disease area, not simply discrete drugs. A program can have many drugs or biologicals at different stages of development each with multiple indications, and all which would factor into the research and development costs for an FDA-approved or licensed therapy. Additionally, since R&D requires paying for failure, Pfizer would assume significant burdens in being required to sort out which costs apply to which products.
 - Thirty days is a wholly inadequate period for manufacturers to gather and submit all the data CMS is requiring for the price setting process. Pfizer recommends that CMS read the statute in a manner that ensures adequate time to gather information and submit data on the 1194(e) factors, and not to adhere to an arbitrary and rigid deadline of October 2nd if there are other, more reasonable ways to interpret the language.
 - **Guidance does not provide transparency, consistency, and predictability.**
 - Rather than describing a "consistent methodology and process," CMS proposes a framework for setting prices that is not transparent, predictable, and there is no way to judge consistence.
 - Among other things, CMS is proposing to place limits on what a manufacturer can use or disclose from CMS' offers, including the ceiling price in the first offer, the information contained in any concise justification provided with an offer, and any information exchanged verbally during the "negotiation" period. These overly broad restrictions go against core First Amendment principles supporting freedom of speech and inhibit transparency and government accountability.

- These policies send the message that CMS wants to make its decisions in secrecy and protect them from outside scrutiny. They also fail to recognize the importance of openness and transparency to maintaining public support for the program. Pfizer urges CMS to abandon its unconstitutional proposals and to adopt evenhanded data policies that respect the freedom of speech and that support transparency – including for Medicare beneficiaries and all industry stakeholders.
- **Guidance lacks sufficient opportunities for patient, provider, and manufacturer input.**
 - The process described in the Guidance signals that CMS intends to provide only the most limited opportunities for stakeholders, such as patients and clinicians, to have input and a voice in this completely new program.
 - CMS should create a process to solicit input and advice from stakeholders including caregivers, patients, and clinicians before the price-setting process occurs. CMS should solicit stakeholder input on topics such as therapeutic alternatives, benefits and impacts of a selected product, how a drug meets unmet needs, subpopulations to consider when evaluating benefits and impacts, and sources of evidence.
 - Manufacturers should be able to meet with CMS before an offer and counteroffer ever would be rejected and counterproposals are issued. During these meetings, CMS should be able to discuss the data CMS uses to determine an MFP and allow manufacturers to provide context to inform the approach used to arrive at calculations, correct data errors, and discuss counter proposals.

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Requirements for Manufacturers of Selected Drugs (Section 40)

Pfizer has significant concerns with many provisions in this section, which focuses on the “Agreement” that manufacturers must enter with CMS under the program.

Primary/Secondary Manufacturer Definition (Section 40)

CMS proposes to define two categories of manufacturers: “primary” and “secondary.” The “primary manufacturer” would be the entity that holds the NDA/BLA for the selected drug. Any other entity involved in the sale or distribution of the product approved under the NDA/BLA -- and meeting the definition of “manufacturer” found at Social Security Act (“SSA”) 1847A(c)(6)(A) -- would be considered a “secondary” manufacturer.

CMS proposes to require the primary manufacturer of a selected drug, among other things, to collect and submit data from any secondary manufacturer, ensure that any secondary manufacturer make the MFP available, and pay any civil monetary penalties for violations (including those stemming from noncompliance by any secondary manufacturer). This proposal is impractical and opens any manufacturer negotiating an MFP with CMS to myriad procedural and legal difficulties. **Pfizer urges CMS to negotiate separate Agreements with any distinct manufacturer.**

CMS’ proposals present legal challenges for so-called “primary” manufacturers. Historically, CMS did not require primary manufacturers to report data on behalf of secondary manufacturers. In fact, in a 2007 rule governing the Medicaid Drug Rebate Program, CMS concluded that requiring one manufacturer to collect and aggregate from a second manufacturer for price reporting purposes could violate antitrust laws

and administrative accounting processes. Pfizer agrees with the concerns that led CMS in 2007 to conclude that such information sharing would be problematic. Thus, Pfizer's view is that compliance with CMS' proposed process to establish "primary" and "secondary" manufacturers for purposes of the MFP could conflict with federal law.

Indeed, many primary and secondary manufacturers are direct competitors and a substantial amount of information and data related to drug development, particularly in the early stages, may be applicable to multiple products and held across different manufacturers -- including competitors. Additionally, while shared research may lead to products developed collaboratively, it also is possible that the research process could lead to development of products that individual manufacturers market separately. CMS' proposals create the potential for negative externalities that CMS must consider, such as whether the process envisioned by CMS may have a chilling effect on future collaborations between manufacturers due to practical challenges, such as primary manufacturers determining it would be overly burdensome to be responsible for collecting and submitting information from secondary manufacturers or, conversely, secondary manufacturers deciding collaborations are overly burdensome or a desire not to share sensitive data with the primary manufacturer. Furthermore, primary manufacturers potentially would have to aggregate data not only from secondary manufacturers, but also from various suppliers for each manufacturer. Pfizer also believes that such data sharing would be problematic.

It also is a misconception to think that compliance monitoring is easier with a single, "primary" manufacturer. Indeed, in addition to the legal considerations noted above, Pfizer believes that CMS' oversight goals would be better accomplished by negotiating separate Agreements with distinct manufacturers. In that way, CMS would not need to monitor compliance through a separate legal entity -- but instead would have a direct Agreement with each manufacturer for that purpose. Indeed, Pfizer believes that the Inflation Reduction Act requires CMS to negotiate separate Agreements with distinct manufacturers. The text of that law indicates that the "Secretary shall enter into Agreements" with "manufacturers" -- thus confirming that Congress did not intend a "primary" / "secondary" manufacturer framework. Any attempt to ensure compliance through only a so-called "primary" manufacturer could rely on multiple steps, difficult processes, and lengthy delays.

Ultimately, requiring a primary manufacturer to collect, aggregate, and submit data from among different entities on selected drugs is misguided and CMS should not adopt this model in final guidance. Instead, we recommend that CMS enter into separate Agreements with each manufacturer that is associated with a selected drug.

Entrance into Agreement with CMS, Compliance with Administrative Actions (Sections 40.1 and 40.5)

The statute instructs CMS to enter into Agreements with manufacturers of selected drugs for IPAY 2026 by October 1, 2023, which is a month after the deadline for CMS to publish the list of selected drugs (September 1). However, in the guidance CMS states that it intends to use the Health Plan Management System (HPMS) to identify relevant points of contact, effectuate the Agreement, and store the Agreement, and that within "5 days following publication by CMS of the list of selected drugs for an initial price applicability year, if the Primary Manufacturer of a selected drug elects to enter into an Agreement with CMS...the Primary Manufacturer must submit to CMS all names, titles, and contact information for representatives authorized to execute the Agreement and conduct the negotiation." CMS also stated that while it will try to make the actual text of the Agreement available in advance, it will not likely seek comments on the Agreement itself. If an Agreement is not fully executed by October 1, 2023, a noncompliance period would begin on October 2, 2023, which could result in excise tax liability.

Pfizer recommends that CMS drop the proposal that manufacturers must enter information into HPMS within 5 days following the publication by CMS of the selected drugs, because the proposal conflicts with the statute, which sets a deadline of October 1 for effectuating the Agreement and it is unreasonable to expect manufacturers to comply with that timeframe. Manufacturers should be afforded the full 30 days to review an Agreement (although we also assert that the statutory deadline is a significant concern) particularly since we are unlikely to have had a chance to review the full text of the Agreement in advance. CMS consistently characterizes the negotiation Agreement as voluntary, which we believe it not an accurate characterization. Manufacturers do not have viable options besides signing the Agreement given the harsh excise taxes that are imposed every day past the required date for Agreement signature or the option to remove all products from Medicare and Medicaid.

We also request that CMS publicly share the Agreement text, for a meaningful public comment period, in order to give patients, providers, and other stakeholders the opportunity to weigh in on the terms of the Agreement and how it may impact access to care. The American people should be able to see what the Agreement entails, especially in IPAY 2026 as this is the first year of the price setting program.

As with any legal contract, manufacturers should not be bound by any ambiguous or undefined terms within the Agreement. The Guidance is untenably vague pertaining to compliance with the Agreement. CMS states in §40.5 that “after entering into an Agreement with CMS...the Primary Manufacturer must comply with requirements determined by CMS to be necessary for purposes of administering the Negotiation Program and monitoring compliance with the Negotiation Program.” This language leaves numerous unstated potential requirements for which manufacturers would be neither legally nor practically privy to prior to signing the negotiation Agreement.

Submission of Data to Inform Negotiation (Section 40.2)

Thirty days is a wholly inadequate period for manufacturers to gather and submit all the data CMS is requiring for the price setting process. While the statute directs manufacturers of selected drugs to submit certain data to CMS by October 2, 2023 (30 days after publication of the list of selected drugs), we believe that CMS has authority to allow room for flexibility in this area. Some of these data points are not currently collected or maintained by manufacturers. Others, such as research and development costs, require manufacturers to look back multiple decades. Still others depend on the cooperation of third-party entities, who would not be penalized in the event CMS’ deadline is not met. Building in additional flexibility would also be to the benefit of CMS as there may be questions or the need to resolve issues around data interpretation. **Pfizer recommends that CMS read the statute in a manner that ensures adequate time to gather information and submit data on the 1194(e) factors, and not to adhere to an arbitrary and rigid deadline of October 2nd if there are other, more reasonable ways to interpret the language.**

Confidentiality of Proprietary Information (Section 40.2.1)

Pfizer urges CMS to take additional steps to secure the vast amount of data manufacturers will be submitting. The Guidance does not provide sufficient details on the confidentiality policy that CMS will adhere to after it receives the proprietary data, and therefore we are troubled by the lack of a public comment period. **CMS’ confidentiality policy should be shared for comments by manufacturers and members of the public and address both use and disclosure of information.**

Though CMS states that the confidentiality policy would be “consistent with existing requirements for protecting proprietary information, such as Exemption 4 of the Freedom of Information Act,” the referenced exemption addresses only the disclosure of information, and not the use of such information. CMS’ vague explanation of a confidentiality policy does not provide any assurances to manufacturers of selected drugs that their proprietary data will be adequately protected.

- **Any confidentiality policy should require that the data submitted by manufacturers are available to the smallest number of personnel possible via a secure portal.**
- **CMS must also propose a cybersecurity policy that addresses necessary safeguards.**
- **Access to data should be inventoried and monitored and data should be immediately destroyed upon the termination of an Agreement.**
- **CMS should also inform manufacturers of any breach or erroneous use of the data and present a solution to remedy any misuse or improper disclosure. CMS should also ensure that referrals are made to the Department of Justice regarding violations of criminal laws prohibiting the publication, divulging, disclosure, or making known in any manner or to any extent not authorized by law, trade secret or confidential commercial information.**

CMS must also clarify that the existence of and status of a pending NDA or BLA, in addition to information contained in a pending NDA or BLA, will be treated as proprietary information under SSA section 1193(c) and as trade secret and/or confidential commercial information that is protected from disclosure under Exemption 4 of the FOIA, 5 U.S.C. § 552(b)(4). This clarification is needed because section 40.2.1 of the Guidance states that “CMS intends to treat the data on prior Federal funding and approved patent applications, exclusivities, and *applications and approvals* under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Services Act as non-proprietary because CMS believes *these data are available publicly* [emphasis added].”

Pfizer disagrees that “these data are available publicly.” Information in pending marketing applications is typically proprietary and highly sensitive and is protected from disclosure by federal law. This sensitivity remains after approval, with much data and information in approved applications remaining protected confidential commercial information and trade secrets exempt from disclosure. Under FDA’s regulations, the existence and status of a pending application, in addition to information contained in a pending NDA or BLA, generally are protected from public disclosure. CMS should consider simply asking the manufacturer to indicate what information is already in the public domain and what, if any, is proprietary and then treat it accordingly, including other manufacturer-submitted data under Section 50.1 of the guidance.

Data Use Provisions and Limitations (Section 40.2.2)

Pfizer urges CMS to abandon the proposal to bar manufacturers from disclosing information and communications exchanged throughout the price-setting process and adopt an approach that promotes transparency and accountability in government decision-making while protecting proprietary and confidential information. Among other things, CMS is proposing to place limits on what a manufacturer can use or disclose from CMS’ offers, including the ceiling price in the first offer, the information contained in any concise justification provided with an offer, and any information exchanged verbally during the “negotiation” period. CMS would prohibit audio or video recording of any oral conversations between CMS and a manufacturer, and even limit use – stating that manufacturers could use government information only for purposes of the Program, and as required by applicable state or federal law. CMS also proposes a “Certificate of Data Destruction,” to be submitted within 30 days of a

drug or biologic no longer qualifying as a selected drug. Under such certificate, a manufacturer would certify that all information received from CMS during the “negotiation” period and potential “renegotiation” period(s), including the initial offer and any subsequent offers, and the concise justification(s), and any of the manufacturer’s written notes or emails pertaining to “negotiation” (or “renegotiations”) with CMS, have been destroyed.

These overly broad restrictions go against core First Amendment principles supporting freedom of speech and inhibit transparency and government accountability. While CMS will publish a justification of MFP at the end of the price setting process, the agency proposes depriving manufacturers of a voice. They also will deny manufacturers the ability to garner year-to-year learnings that will be important to the effective implementation of and manufacturer compliance with the Program. These policies send the message that CMS wants to make its decisions in secrecy and protect them from outside scrutiny. They also fail to recognize the importance of openness and transparency to maintaining public support for the program.

Pfizer urges CMS to abandon its unconstitutional proposals and to adopt evenhanded data policies that respect the freedom of speech and that support transparency --including for Medicare beneficiaries and all industry stakeholders.

Effectuation of the MFP (Section 40.4)

Under section 1193(a) of the SSA, manufacturers entering into an Agreement with CMS must provide access to the MFP for selected drugs that are covered under Part D to (1) MFP-eligible individuals and (2) pharmacies, mail order services, and other dispensers with respect to such MFP-eligible individuals who are dispensed such drugs. CMS intends to require primary manufacturers to provide access to the MFP in one of two ways: (1) by ensuring that the price paid by the dispensing entity is no greater than the MFP; or (2) by providing retrospective reimbursement for the difference between the dispensing entity’s actual acquisition cost and the MFP.

Pfizer is deeply concerned with CMS’ proposed two options, absent the necessary supporting supply chain infrastructure and data reporting necessary for manufacturers to verify MFP claim eligibility and 340B drug status. **Pfizer requests that CMS articulate viable processes by which manufacturers of selected drugs will be provided access to Medicare claims data to verify claims for prospective and retrospective MFP discounts. To assist CMS with this process, we have included backgrounder in the Appendix to this letter which more fully describes concerns and potential solutions for manufacturers to provide access to the government-set price (MFP).**

Specifically, Pfizer urges CMS to:

- **Provide manufacturers of selected drugs with Part D prescription drug event (PDE) records to ensure that the patient is MFP-eligible.**
- **Remove the requirement for manufacturers to provide reimbursement to intermediate entities within 14 days.**
- **Utilize wholesale acquisition cost (WAC) to define the amount of MFP discounts rather than actual acquisition cost (AAC).**
- **Assign a third-party administrator to oversee the MFP effectuation process for manufacturers that elect to provide retrospective reimbursement to dispensing entities.**

We are very concerned about the lack of assurance that manufacturers will receive proof of MFP eligibility and 340B drug status prior to reimbursement. A manufacturer will need appropriate data to provide 340B covered entities (CEs) with the lesser of the MFP and 340B ceiling price, as well as to

prevent payment of both an MFP statutory discount and a 340B discount on the same unit as is expressly prohibited under the MFP/340B nonduplication clause.

Additionally, the requirement for manufacturers (who choose the retrospective route of effectuating the MFP) to reimburse applicable intermediate entities within 14 days is wholly unattainable without eligibility verification. Instead, to meet the required payment deadline to pharmacies and other dispensers, manufacturers could contract with intermediate entities to facilitate payments to pharmacies, provided those intermediate entities are given access to claims-level transaction data. However, manufacturers need more time than the 14 days proposed by CMS to review claims and verify patient eligibility for the MFP. Thus, we strongly recommend that CMS eliminate the requirement to reimburse intermediate entities within 14 days and instead provide flexibility for intermediate entities and manufacturers to develop processes and set contractual terms related to timing of payment.

Another issue with effectuating MFP is CMS' proposed use of actual acquisition costs (AAC) to determine the magnitude of the discount. AAC is an opaque and inappropriate metric to define the MFP discount that manufacturers must reimburse to dispensing entities, as it is difficult to track and is only known to the dispensing entity. Additionally, perverse contracting incentives could result from dispensing entities reporting the AAC for each prescription, as plans or PBMs could undercut a pharmacy in reimbursement negotiations if the AAC were known to the plan or PBM. CMS should define a retrospective MFP discount using a widely available metric such as WAC.

Finally, we urge CMS to improve effectuation of the MFP and minimize stakeholder burden by designating a third-party administrator (TPA) to facilitate this process for manufacturers choosing a retrospective approach. This will best ensure consistent patient access to the MFP at the point-of-sale, enable full reimbursement to pharmacies through a standardized process within the 14-day timeframe proposed by CMS, protect program integrity, promote efficiency and accuracy, and minimize stakeholder burden.

Nonduplication with 340B Ceiling Prices (Section 40.4.1)

The statute includes a provision that prevents duplicate MFP and 340B discounts for selected drugs. In section 40.4.1 of the Guidance, CMS states that a primary manufacturer is required to provide access to the MFP to 340B covered entities (CEs) if the MFP is below the 340B ceiling price for a selected drug when the CE (or a pharmacy on its behalf, in appropriate cases) dispenses a selected drug to a 340B patient of the CE who is also a Medicare beneficiary. CMS further states that if the 340B ceiling price is "subsequently determined" to be below the MFP, then the manufacturer is responsible for providing the 340B CE the difference between the MFP and 340B ceiling price.

However, Pfizer has significant concerns that these proposed requirements do not describe the nonduplication clause correctly and conflict with CMS' proposal to require reimbursement within 14 days. In fact, this is likely to result in manufacturers providing duplicate discounts instead of preventing them.

Pfizer asks that CMS revise its guidance to address the potential for duplicate MFP and 340B discounts. Solutions may include (1) clarifying that manufacturers can choose to make the MFP the default payment and converting the 340B discount for selected drugs to a rebate to the covered entity or (2) requiring that 340B units be identified at the point of sale.

Most 340B drugs are managed in a virtual inventory and replenishment model in which dispensing entities receive the medication upfront at the 340B price and virtually track patient 340B eligibility. The software used for the 340B virtual inventory system is prone to lags in identifying 340B-eligible claims, rendering dispensing entities unable to determine the appropriate acquisition price in time for manufacturers to meet the 14-day reimbursement requirement. As a result, manufacturers will likely be liable to provide unlawful duplicate discounts (e.g., MFP and 340B ceiling price) absent further action from the agency.

If CMS cannot resolve these critical issues, we urge you to withdraw sections 40.4 and 40.4.1 from the revised Guidance and continue to work with the appropriate stakeholders to develop a workable solution.

Identifying Units Subject to 340B Agreements

For manufacturers to provide the lower of MFP or the 340B ceiling price to 340B patients who are Medicare beneficiaries, it is critical that CMS adopt a methodology by which all Part D claims that are subject to 340B pricing are identified accurately and in a timely manner. **Pfizer supports CMS' proposal included in the Part D inflation rebate guidance to require all PDE and pharmacy claims to append a 340B modifier. Further, a non-340B modifier should be required such that every claim reports 340B status.** This requirement would align with CMS' approach for the discarded drug modifier in the Medicare Part B program. However, Pfizer is concerned that even with a requirement for claims to include a 340B or non-340B modifier, compliance by covered entities may not be sufficient to ensure that all 340B claims are identified.

Negotiation Factors (Section 50)

The statute requires CMS to “develop and use a consistent methodology and process” to negotiate the MFP. Thus, all negotiations should be subject to a clear and predictable framework. Sections 50 and 60 of the Guidance describe numerous, closely related elements of the price-setting process (statutory factors, price setting methodology and process, respectively). Unfortunately, Pfizer believes that the process described by CMS in these sections does not create the required clear framework envisioned by Congress.

The lack of specificity in how CMS will define and weigh individual factors, combined with an opaque process, results in a price setting process that will appear subjective and arbitrary in direct violation of the legal requirement for a clear and reasonable framework. We urge CMS to make changes to provide needed clarity and specificity in the MFP methodology and factor definition.

Fundamentally, we are concerned that CMS has proposed an approach that:

- defines the negotiation factors in ways that seem explicitly designed to drive the MFP to excessively low “cost-plus” pricing levels;
- doubles down on the inherent flaws in the statute’s unprecedented inclusion of “R&D recoupment;” and
- penalizes rather than rewards manufacturer investments in continued R&D following a drug’s approval.

Requirements for Submission of Manufacturer Submitted Data Generally (Section 50.1)

In section 50.1 of the Guidance implementing the “manufacturer-specific data” provisions of the IRA, CMS states that it intends to require a primary manufacturer to submit data regarding R&D costs of the primary manufacturer and whether the primary manufacturer has recouped those costs; current unit costs of production and distribution; prior federal financial support for the drug’s discovery and development; data on pending and approved patent applications, patent exclusivities, and NDA/BLA approvals; and market data and revenue and sales volume data in the U.S. for the primary and secondary manufacturer. Appendix C of the Guidance includes a list of definitions that describe the data to be collected for the Program.

CMS proposes to require the primary manufacturer to aggregate data from both the primary manufacturer and secondary manufacturer on the non-FAMP, current unit costs of production and distribution, market data, and revenue and sales volume. As noted earlier in our comments, it is not workable for primary manufacturers to report these data on behalf of secondary manufacturers since primary manufacturers may lack access to such data from secondary manufacturers, either legally or practically. **In addition to rescinding its proposal to adopt the primary and secondary manufacturer model – and instead enter into separate Agreements with each manufacturer that is associated with a selected drug – Pfizer, at a minimum, strongly recommends CMS exercise its discretion to allow additional data submission after the October 2, 2023 deadline.**

Pfizer also notes that CMS can obtain some of the requested information from government sources to alleviate unnecessary burden on manufacturers. **For example, Pfizer recommends that CMS obtain information about approved patent applications from the FDA’s Orange and Purple Book listings, information about approved applications from Drugs@FDA, and information about unexpired regulatory and patent-based exclusivities for NDAs from the FDA Orange Book, and explicitly allow companies to reference such sources in their submissions to CMS.** Conversely, manufacturers should be able to provide as much supporting information as required to support the negotiation process. **Accordingly, Pfizer requests that CMS abolish any text limits (on the data submission forms or portals) for manufacturer submissions to ensure we can submit all information relevant to the negotiation.**

Research and Development Costs (Appendix C)

With regard to R&D costs and the recoupment of investment, CMS states in the Guidance that it will review a combination of costs incurred by the primary manufacturer for all FDA-approved indications of a drug, such as basic pre-clinical research costs, post-Investigational New Drug (IND) application costs, FDA Phase IV clinical trials, post-marketing trials, abandoned and failed drug costs, and all other R&D costs. CMS proposes to calculate “recoupment” of R&D costs by comparing them to global, total lifetime net revenue for the selected drug. CMS would then increase or decrease the preliminary MFP it calculates depending on whether costs have been “recouped.”

This approach is problematic for several reasons. First, it is important to understand that manufacturers and investors typically invest in research & development for “programs” in a specific disease area, not simply discrete drugs. A program can have many drugs or biologicals at different stages of development each with multiple indications, and all which would factor into the research and development costs for an FDA-approved or licensed therapy. This can include thousands and sometimes millions of compounds that could be screened early in the research and development process, going back many years, with a success rate of less than 12%. And once a drug is on the market, it’s not a guarantee that it will be a huge

commercial success due to many factors, including significant competition from other medicines. It is the revenue that comes from the commercial successes that support continued investment in the high-risk effort to discover new medicines and help to recoup costs of the many failures across an entire portfolio.

In addition, the task of submitting the R&D costs for the selected drug will be extremely difficult if not impossible for manufacturers to perform since, as we just described, R&D costs are a difficult metric to capture. The cost of delivering a drug to market reflects only a fraction of total pipeline expense, not just the direct costs for a successful approval. R&D costs should include all costs required to discover and market a drug from discovery through launch and end-of-life, which includes R&D costs, support costs, and financing.

It is extremely difficult for Pfizer to completely and accurately account for such a wide variety of costs. Attributing R&D costs to a particular drug or combination of drugs presents a significant challenge. Pfizer pursues multiple drugs simultaneously for the same indication -- to identify the highest impact medicine for patients. Additionally, since R&D requires paying for failure, Pfizer would assume significant burdens in being required to sort out which costs apply to which products. Additionally, support for R&D comes from a range of functions including commercial, medical, value and access, technology, finance, strategy, and operational support currently not necessarily captured in R&D expenses.

In addition to these difficulties, CMS would require Pfizer to account for secondary manufacturer R&D costs. This would require that Pfizer - within 30 days - capture all of their investments that could have been made over 20 years ago and recorded through any number of various technologies or paper forms. To provide this level of detail is an extremely challenging task.

In light of all these challenges, we recommend that CMS place minimal weight on this factor and specify that whether a manufacturer “recouped” its costs will not be used to reduce an MFP that is more appropriately determined on the basis of a drug’s therapeutic and clinical attributes. In addition, in lieu of the proposed standardized definitions, CMS should allow manufacturers to use reasonable assumptions (with accompanying justifications) regarding the information they submit on manufacturer-specific data related to R&D costs. Further, we urge CMS to modify the proposal to limit required submission of R&D costs to data available to the manufacturer that can be directly attributable to the selected drug, while allowing companies to voluntarily provide supplemental data.

Current Unit Costs of Production and Distribution (Appendix C)

The Guidance defines costs of production to include all direct and indirect costs related to purchasing raw ingredients, including intermediates, active pharmaceutical ingredients, excipients, and other bulk chemicals; formulating and preparing the finished drug product; performing quality control and testing of the drug; and operating costs for personnel, facilities, transportation, any importation, and other expenses related to preparing the finished drug product. Distribution costs would include all direct and indirect costs related to packaging and materials; labeling; shipping to any entity that acquires the drug from the primary or secondary manufacturer; and operating costs for any of the above. Current unit costs would include only costs incurred by the primary and secondary manufacturer and only units produced and distributed for sale in the U.S. R&D costs and marketing costs would not be included.

Pfizer is concerned with CMS’ definition of production and distribution costs for a number of reasons, including that Pfizer may not be able to obtain some of these data from secondary manufacturers or our supply chain partners. **Pfizer requests that CMS allow manufacturers discretion to include which**

production and distribution costs are available and permit manufacturers to provide a narrative rationale for any factor they may be unable to include.

Prior Federal Financial Support (Appendix C)

The Guidance defines prior federal financial support to include tax credits, direct financial support, grants or contracts, and any other funds provided by the federal government to support discovery, research, and/or development of the selected drug – all during the time period from when initial research began or when the drug was acquired by the primary manufacturer, through the date the most recent NDA/BLA was approved. CMS states that it may consider decreasing the preliminary price if funding for the drug’s discovery and development was received with federal financial support.

Pfizer objects to CMS’ proposal to include tax credits as “federal financial support” for the purpose of reducing drugs’ MFP. This runs contrary to the goal of these tax credits. Credits such as the orphan drug tax credit promote American innovation, foster American expertise, and help manufacturers develop products that save lives. These credits don’t necessarily ladder up to a specific drug product, which further complicates accounting of them in R&D costs. Congress established these credits with specific innovation and economic goals, and their inclusion as a factor to drive down the MFP runs contrary to these broader objectives.

Pfizer requests that CMS remove tax credits from the definition of federal financial support. Pfizer also requests that CMS limit consideration of federal financial support to only products with a patent application containing a Government Interest Statement and/or research where a patent assignee was a government agency.

Patents, Exclusivities, and Approvals (Appendix C)

In the Guidance, CMS considers relevant patents to be those that are pending or approved and linked to the selected drug as of September 1st, 2023, as well as pending and approved applications for which a claim of patent infringement could reasonably be asserted against a person engaged in the unlicensed manufacture, use, or sale of the selected drug. CMS notes that FDA exclusivity periods include Orphan Drug Exclusivity and Pediatric Exclusivity. CMS states that it will consider the length of the available patents and exclusivities before the selected drug may no longer be single source and may consider decreasing the preliminary price if the selected drug has patents and exclusivities that will last for a number of years.

Pfizer opposes CMS’ proposal to decrease the MFP for selected drugs that have remaining patents and exclusivities. Patent rights are a form of IP protection and are critical to the continued investment in R&D, including for new medicines and improvements for existing medicines. CMS’ proposal to penalize manufacturers for the lengthy, costly, and risky R&D (including post-approval R&D) that has resulted in patents and exclusivities will undermine U.S. leadership in biopharmaceutical innovation and weaken the intent of the IP system. As a matter of course, drugs selected for price setting at 7 or 11 years will have remaining patents and exclusivities. In fact, any remaining patents and exclusivity – including exclusivities from innovations such as for orphan products and post-approval innovations – should serve to increase the MFP in order to reflect these dynamics.

Additionally, CMS should acquire patent data not from manufacturers, but from public Orange and Purple Book listings as other data collection is already a massive burden on manufacturers and the 30-day timeframe is extremely short.

Finally, CMS should explicitly confirm that “pending applications” for submissions purposes do not include abandoned applications, which would not be relevant for CMS’ price setting process and are considered neither pending nor approved patent applications. CMS should further clarify that manufacturers are not required to submit non-public patent information, including information about pending applications that have not been published, given the highly confidential nature of this information. Manufacturers should also be permitted to refer CMS to the Orange and Purple Book for exclusivity data and Drugs@FDA for information about approved applications. Manufacturers could then supplement those sources with information about pending applications, such as ongoing R&D efforts which may result in additional periods of exclusivity (pediatric programs or new indications).

Market Data and Revenue and Sales Volume Data (Appendix C)

CMS proposes to require that manufacturers report more than 20 metrics relating to drug prices and sales:

- WAC unit price
- National Council for Prescription Drug Programs (NCPDP) billing unit standards
- 340B ceiling price
- Medicaid Best Price
- Average manufacturer prices (AMP)
- 340B prime vendor program price
- Federal supply schedule (FSS) price
- Big Four price
- U.S. commercial average net unit price, without patient assistance (and possibly with patient assistance) and “best”
- Manufacturer average net unit price to Part D Plan sponsors without patient assistance (and possibly with patient assistance) and “best”
- Total U.S. gross revenue
- Total U.S. net revenue with and without patient assistance
- Quarterly total U.S. unit volume.

In most cases CMS would require the primary manufacturer to aggregate its own data on the selected drug from both the primary manufacturer and data from any secondary manufacturer. Like all the other submission requirements, the Guidance specifies that all of these data with explanations must be submitted to CMS within 30 days of selection – by October 2, 2023.

Pfizer is concerned with the broad and burdensome requirements to submit market data, revenue, and sales volume data. Along with many currently available prices, manufacturers would have to report a new U.S. commercial average net unit price and a manufacturer average net unit price to Part D Plan sponsors in three ways (i.e., with patient assistance, without patient assistance, and best price). **Pfizer requests that CMS withdraw these new metrics in revised guidance.**

There are multiple problems with these new metrics:

- Flawed assumptions about manufacturer patient assistance: patient assistance is financial assistance intended to reduce patients’ out-of-pocket costs and is not considered a price

concession offered to customers. In other words, patient assistance does not constitute “market” data under SSA §1194(e)(1). But this is the rubric under which CMS would require manufacturers of selected drugs to report their patient assistance amounts.

- Guidance is silent (and thus creates additional confusion) on whether a “patient assistance program” is meant to include a manufacturer’s charitable free drug programs (which it should not). The fact that CMS refers to “patient assistance” in a Part D context where manufacturers do not provide cost-sharing assistance to patients causes further questions about what CMS means by “patient assistance.” Yet there is language in the data elements ICR that seems to consider only “coupons and copay assistance” as the patient assistance that CMS is asking manufacturers to report.

If CMS does not withdraw these new metrics, we ask CMS to delete all items asking for manufacturers to report “patient assistance” from the guidance (and the related data elements ICR). Failing that, we request that CMS explicitly clarify that (1) “patient assistance program” does not include manufacturer charitable free drug programs, and (2) wherever a definition does not include the qualifier “without patient assistance program,” that definition excludes manufacturer charitable free drug programs.

CMS also should clarify treatment of products that may have multiple WAC prices per NDC-9. Pfizer anticipates scenarios in which some products do not have a single WAC price per lowest dispensable unit. For example, there could be a product with the same strength and form (which would be the same NDC-9 – for example, 20 mg tablets) but a bottle of 100 tablets has a WAC of \$100 and a bottle of 1,000 tablets has a WAC of \$900.

Quality Adjusted Life Years and Cost Effectiveness Analysis (Section 50.2)

Pfizer appreciates that CMS will not use QALYs in determining MFPs, but requests that CMS be more specific about the prohibition. While we agree with CMS’ statement that the language set forth in the IRA prohibits CMS’ reliance on QALYs or similar metrics, we are concerned that CMS fails to reference the existing prohibition on Medicare reliance on QALYs or similar metrics found in the SSA. Specifically, the Affordable Care Act prohibited Medicare from making decisions based on QALYs and similar metrics, a key statutory measure that CMS should explicitly mention in revised guidance. This prohibition would prevent CMS from using QALYs as part of its determination of MFPs, including in a “life extension context.” We ask CMS to explicitly acknowledge this additional statutory prohibition in its revised Guidance, and refrain from using QALYs or any similar metric, in any context.

QALYs are discriminatory against disabled and elderly Medicare beneficiaries -- a concern reflected in CMS’ Guidance. In addition, QALY-based cost effectiveness analyses often assign lower value to Black lives and undervalue other communities of color, including due to the lower life expectancy within communities of color.⁴ The government price setting process be careful not to use methodologies that exacerbate existing racial and ethnic disparities in health.

Pfizer is concerned by CMS’ statement that it will use research that has “separated” evidence or assessments based on QALYs from other outcomes. We believe this is not realistic, and CMS should require that any entity submitting information to CMS attest that it removed QALY-based research, including any comparative effectiveness research that may have been intrinsically affected by use of QALYs in a related analysis.

⁴ Arias E, Tejada-Vera B, Ahmad F, Kochanek KD. (2021). “Provisional Life Expectancy Estimates for 2020.” Vital Statistics Rapid Release.

Beyond our concerns about QALY-based assessments, we urge CMS to commit to not relying on or over-emphasizing cost-effectiveness analyses (CEA) to determine the price for a selected drug, because it risks further discriminating against underserved and underrepresented people of color who are already at higher risk of not receiving the care they need. In addition, CEA based on any metric can present significant concerns beyond those issues related to discrimination, as it often fails to capture benefits and impacts that matter to patients or patient subgroups.

Standards for Review of Literature and Research (Section 50.2)

CMS should specify robust standards for literature and research reviews and clarify that internal analytics will be required to meet quality standards like those of outside analysis. CMS can borrow standards from other groups such as academic organizations (e.g., the International Society for Pharmacoepidemiology (ISPE) and the International Society for Pharmacoeconomics and Outcomes (ISPOR)) that have developed standards and best practices for analyses and health technology assessments. Medicare drug price setting is too important for CMS to not have robust and public analysis standards.

Standards for Third Parties Providing Evidence (Section 50.2)

The Guidance states that CMS will “consult subject matter experts as part of its process to set [drug prices] for selected drugs, in addition to considering evidence from “the Primary Manufacturer and members of the public, including other manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested parties.”

We urge CMS to develop robust standards for the third parties CMS engages or that serve as resources to provide evidence on selected drugs and assist CMS in the price setting process. Such standards should ensure these organizations apply methodological rigor in their approach and have a patient-centered focus to their research. CMS should generally avoid relying on any technology assessment organizations that cannot demonstrate clear independence and patient-centeredness. Further, while CMS can be considered a payer, the agency has a broader mission than other payers. Thus, CMS should exclude organizations with a payor-focused mission or funding as well as organizations that historically focus on CEA that relies on QALYs when determining a selected drug’s MFP. This is important because of statutory prohibitions against certain types of CEA as well as the need to avoid analysis driven by a payor focus on cutting costs over patient needs that discounts clinical and non-clinical benefits that matter to patients, caregivers and society.

At a minimum, CMS should publicly disclose the identity and contributions of third parties and ask for them to disclose potential conflicts of interest.

Consideration of Real-World Evidence (RWE) (Section 50.2)

Pfizer appreciates that CMS will consider RWE in setting Medicare drug prices. However, CMS should clarify the standards that CMS will use and how RWE will be weighed. Real-world evidence can come from myriad sources, including electronic health records, claims data, and patient surveys. CMS should consider evidence from all these sources, but the agency must establish clear standards for the type of RWE and the weighting of these data. **Real-world evidence can help provide a more accurate**

assessment of the value to patients and society of Pfizer's innovations, and we hope CMS will strongly consider rigorous RWE generated after FDA approval of a drug.

Consideration of Specific Patient Populations (Section 50.2)

CMS states that it will consider research on and RWE relating to Medicare populations -- including individuals with disabilities, end-stage renal disease (ESRD) and aged populations -- as particularly important. In addition, CMS will prioritize research specifically focused on these populations over studies that include outcomes for these populations, but in which these populations were not the primary focus. CMS states that it will consider the effects of the selected drug and its therapeutic alternative(s) on specific populations, including individuals with disabilities, the elderly, the terminally ill, and children.

While the sub-populations listed above are important, Pfizer urges CMS to consider all relevant subpopulations to fully understand the value of the selected medicines. Other patient subpopulations differ in therapy preferences and responses as well as the value they place on various outcomes. For example, studies have long shown that patients place significant emphasis on benefits other than prolonged survival or cost, although these preferences vary considerably depending on factors such as type and severity of disease and individual life circumstances.

Negotiation Process (Section 60)

Price Setting Methodology

Section 1194 of the SSA, requires a “consistent methodology and process” for setting MFPs, and that these prices be “fair.” However, CMS’ Guidance provides no assurance that the Agency will meet this standard. Rather than describing a “consistent methodology and process,” CMS proposes a framework for setting MFPs that is not transparent, predictable, and there is no way to judge consistence. Furthermore, the process for price-setting signals that CMS intends to provide only the most limited opportunities for stakeholders, such as patients and clinicians, to have input into the process.

CMS’ starting point for the initial offer amounts to therapeutic reference pricing and gives CMS the ability to make judgments about clinical similarity without sufficient opportunities for stakeholder input. We note that therapeutic reference pricing, which resembles the “least costly alternative (LCA)” policies previously attempted by CMS, would give CMS authority to make judgments about clinical “similarity” for a broad range of medicines. It could also overlook significant differences in the needs of patients, many of whom don’t fit value judgments based on broad, average results.

We are concerned this will result in prices that don’t reflect the value these medicines bring to patients and society, and thus Pfizer recommends that CMS undertake a scoping process and engage with manufacturers prior to determining an initial offer. As discussed further below, we also recommend that CMS leverage a Multi-Criteria Decision Analysis methodology as part of its approach to establishing a price for selected drugs. Such a methodology should be patient-centered and consider the holistic value of a medicine, including humanistic and societal benefits. We recommend that CMS follow several critical principles of value assessment in its methodology for establishing an MFP, including ensuring that the methodology is patient-centric, is transparent, takes a holistic view of value, recognizes that value is dynamic, is supportive of innovation, and addresses access.

The scoping document should be informed by a range of key stakeholders and a public consultation period at the start of each selected drug evaluation. It should include:

- 1) therapeutic alternative(s) considered for each indication for selected drugs and the rationale for selection**
- 2) patient population and subgroups to be considered**
- 3) definition(s) of unmet need for each indication of selected drugs**
- 4) full range of benefits and impacts considered for each indication**
- 5) internal process and rationale for determining which benefits and impacts were included**
- 6) list of each stakeholder consulted**

This document would clarify how each treatment will be assessed and under what conditions. It would also offer an opportunity to develop a more advanced and detailed methodology to support the negotiation process. For example, it remains unclear how CMS will assess “clinical benefit” and how this will translate to the preliminary price. In the document, CMS should clarify the methodology it will use to assess clinical benefit across different sources of evidence (e.g., randomized control trial, real-world data, indirect treatment comparison, etc.) and expert opinions.

The negotiation process will have significant implications for patient access and affordability and should include a clear and precise process for patient involvement. Patients offer a unique perspective regarding health conditions, existing therapies, and the value therapies bring – perspectives that CMS should take into account during the negotiation process. Simply asking stakeholders to provide information through an ICR is an insufficient means of engaging stakeholders on this key issue.

CMS should create a comprehensive and deliberative process to solicit input from patients and caregivers at the start of the price setting process and invite comprehensive feedback from patients and caregivers on a range of elements of its decision-making, including but not limited to 1) identification of therapeutic alternatives or comparators for a selected drug, 2) benefit and impacts of a selected drug, 3) the extent to which CMS has determined a selected drug meets and unmet need, 4) specific subpopulations to consider when determining the benefits and impacts of a selected drug, and 5) sources for evidence supporting CMS decision-making and weighing of evidence.

CMS also relies heavily on the federal supply schedule (FSS) or “Big 4” prices, which are not intended to create pricing benchmarks for drugs. This kind of domestic reference pricing is not appropriate for a number of reasons. Average prices across government programs cannot be compared, due to varying storage, distribution, and dispensing practices. Additionally, FSS and “Big 4” prices already reflect inflation and rebates provided and using them as a benchmark would lead to double counting inflation. This approach was also rejected during the debate on the IRA when Senator Bernie Sanders offered an amendment to tie drug prices in Medicare to those used in the U.S. Department of Veterans Affairs (VA). This amendment failed overwhelmingly by a vote of 99 to one.

Pfizer recommends that CMS adopt a methodology in the initial years of the program that acknowledges the extraordinary complexity of establishing a price setting program for the first time -- where all relevant stakeholders do not have experience in this type of novel government price setting program. There is also a tremendous burden on manufacturers to submit data and engage in this complicated process with little information or advance notice. Given these factors, we recommend CMS set the MFP at the statutory ceiling price starting with IPAY 2026 and for several subsequent price applicability years.

Weighting of Factors

The statute establishes two sets of factors that CMS must consider when determining the offers and counteroffers to set the price for the selected drug: “manufacturer-specific data” and evidence regarding alternative treatments. But it does not specify how CMS should determine an initial offer nor how or to what degree each factor should be considered. **We believe CMS should clarify in the Guidance how it will use its discretion in considering and weighting the factors, and we strongly urge CMS to place greater emphasis on the factors related to the benefits products offer to patients, caregivers, and society.**

Conversely, CMS should place less importance on factors that would stifle innovation if overweighted. This includes most of the factors listed in section 1194(e)(1), such as cost of production, costs of R&D, and federal funding toward the development of a selected drug. **CMS should avoid a “cost recovery model” where manufacturers only recoup the cost of producing the drug. In order to mitigate the effect of government price setting on innovation, factors used to support a higher government-determined price should include patent protections, regulatory data exclusivities, labeled and pending indications, and ongoing clinical development programs.**

Therapeutic Alternatives

CMS states that for IPAY 2026 it will identify the selected drug’s FDA-approved indications that are neither excluded from coverage nor otherwise restricted. CMS will then identify pharmaceutical therapeutic alternative(s) for each indication of the selected drug, using data submitted by the primary manufacturer and the public, along with widely accepted clinical guidelines and peer-reviewed studies. CMS also will consider clinical evidence via literature searches.

We urge CMS to utilize manufacturers, clinicians, and patients as the primary resources for determining therapeutic alternatives. The clinically appropriate standard should be used for decision making, meaning CMS should (1) engage with manufacturers on potential therapeutic alternatives and comparators, (2) reference clinician guidance as a resource, (3) reference recognized, science-based, evidence-informed resources to identify alternatives and (4) engage with patients/patient groups.

Additionally, CMS should not consider off-label use when evaluating therapeutic alternatives. Inclusion of off-label use could diminish the value of drugs that were approved for the indication and impact future innovation.

Benefits and Impacts

In assessing comparative effectiveness between a selected drug and therapeutic alternative(s), CMS plans to identify outcomes to evaluate for each of the selected drug’s indications and consider the safety profiles. When evaluating clinical benefits of the selected drug and its therapeutic alternative(s), CMS intends to consider health outcomes, intermediate outcomes, surrogate endpoints, patient-reported outcomes, and patient experience.

Pfizer urges CMS to consider the benefits and impacts of a selected drug that are important to patients, caregivers, and society. In evaluating relative clinical benefit, Pfizer urges CMS to consider patient-centric methodologies that are complete, comprehensive, and fit-for-purpose, as opposed to QALY-based approaches. Multi-criteria decision analysis (MCDA), for example, is a

widely recognized and accepted methodology for aggregating different dimensions of value for patient-centered value assessment. MCDA can account for a range of perspectives and values such as those outlined by CMS: health outcomes, intermediate outcomes, “validated” surrogate endpoints, patient-reported outcomes, and patient experience. Incorporating the patient experience is critical to ensuring clinical benefit is captured however, it is important to ensure we also capture impacts to others effected by the disease/condition such as family members and informal caregivers. Importantly, MCDA addresses many of the concerns of discrimination against disabled and elderly patients that are inherent in utility-based metrics such as QALYs.

Following the negotiation data elements information collection request (ICR) and before CMS’ initial offer, CMS should have direct conversations with manufacturers and stakeholders to share the benefits and impacts it flagged as meaningful. Additionally, in its explanation of a selected drug’s price, CMS should publicize the benefits and impacts considered in the determination of a drug’s price, the process for determining benefits and impacts, evidence sources, and how each benefit and impact determined the final price.

Cost of Selected Drug and Therapeutic Alternatives

The statute includes as a factor “the extent to which such [MFP] drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives,” to the extent such information is available.

We urge CMS to interpret that language broadly, to include a range of direct and indirect costs and cost savings associated with appropriate use of a selected drug. For example, costs should include real-world costs, such as lost wages for caregivers, costs of traveling to a center of excellence for diagnosis and drug administration or acquisition, and the cost of any side effect burden. And medicines not only improve and save lives, but also frequently help avoid other, often costly, health care services, such as emergency room visits, hospital stays, surgeries, and long-term care.

In addition, data CMS uses to understand drug costs should reflect the true net costs after rebates, including those paid to Medicare Part D plans and as well as the 340B program.

Clinical Benefit & Unmet Medical Need

CMS states that it will consider a selected drug as filling an unmet medical need if it treats a disease or condition where there are very limited or no other treatment options.

This is a very narrow definition of unmet need and assumes a one-size-fits-all approach, not considering differences between patient groups and subgroups. Determining unmet need should be a collaborative process with a range of stakeholders -- and the patient at the center. The assessment of unmet needs should be carefully evaluated as the treatment is now multiple years post launch and has been bridging an important unmet need gap throughout this time. That is, CMS should consider the status of “unmet need” at the time the drug was first FDA approved. Unmet need should also reflect morbidity and mortality for the respective therapeutic area. If CMS fails to fully acknowledge innovation that addresses unmet patient needs, it will send signals that disincentivize ongoing innovation in areas where patients desperately need options.

CMS should look to the FDA definition of unmet need: FDA defines unmet medical need as “a condition whose treatment or diagnosis is not addressed adequately by available therapy” that includes either “an immediate need for a defined population” or “a longer-term need for society.” FDA further clarifies that such a drug will treat a condition:

- where there is no available therapy;
- where there is available therapy, but the drug presents additional benefits; and
- where the only available therapy was approved under the accelerated approval program and clinical benefit against the primary endpoint has not yet been verified.

Furthermore, CMS should recognize other types of unmet need, including, but not limited to:

- personalized medicines for certain subpopulations;
- progress against rare and hard-to-treat illnesses;
- treatments that improve patient adherence and quality of life;
- need for additional treatments in a therapeutic area, such as a curative treatment;
- treatments that improve the health of underserved and vulnerable communities who face health disparities, particularly communities of color;
- treatments that benefit multiple common comorbidities at once; and
- the stepwise nature of progress in which significant gains for patients are achieved via advances that build on one another.

Therapeutic Advance

The statute requires CMS to consider “[t]he extent to which such drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives.”

For the purpose of encouraging R&D and mitigating against the negative impacts of this law to innovation, CMS should look at the alternatives that were available at the time of the drug’s approval. At a minimum, it should weight such drugs higher than later introduced alternatives.

In addition, CMS could consider examples within existing Medicare reimbursement policy that can assist in defining and assessing selected drugs against this criterion. For example, one appropriate factor would be the **New Technology Add-On Payment (NTAP)** designation, which exists to ensure adequate reimbursement for certain new products that demonstrate, among other things, enhanced clinical improvement over existing technologies. In order to receive an NTAP designation, a product must demonstrate a substantial clinical improvement over existing services or technologies (in addition to two other distinct criteria), which is defined as “an advance that substantially improves, relative to...technologies previously available, the diagnosis or treatment of Medicare beneficiaries.”

Another resource for determining whether a treatment represents a therapeutic advance could be highly credible, physician-driven oncology compendia, such as the **National Comprehensive Cancer Network (NCCN)’s Drug and Biologics Compendium**. CMS already relies on this Compendium in other contexts.

Manufacturer Engagement

CMS states that if the primary manufacturer does not accept CMS’ written initial offer and proposes a written counteroffer, which is not accepted by CMS, CMS will invite the primary manufacturer to an in-

person or virtual meeting that would take place within 30 days of CMS' receipt of the primary manufacturer's written counteroffer. After this initial meeting, each party would have the opportunity to request one additional meeting, for a maximum of three meetings between CMS and the primary manufacturer. In addition, all meetings must occur during a narrow time period – approximately four months' time between the primary manufacturer's written counteroffer to CMS and the end of the price setting period.

We urge CMS to allow manufacturers to engage with CMS much earlier in the process. Manufacturers should be able to meet with CMS before an offer and counteroffer ever would be rejected and counterproposals are issued. During these meetings, CMS should be able to discuss the data CMS uses to determine an MFP and allow manufacturers to provide context to inform the approach used to arrive at calculations, correct data errors, and discuss counter proposals.

Patient/Clinician Engagement

As stated earlier in our comments, we urge CMS to create a process to solicit input and advice from stakeholders including caregivers, patients, and clinicians before the price-setting process occurs. CMS should solicit stakeholder input on topics such as therapeutic alternatives, benefits and impacts of a selected product, how a drug meets unmet needs, subpopulations to consider when evaluating benefits and impacts, and sources of evidence. CMS' current approach, particularly for patient and provider groups, is particularly challenging for patient and provider groups and will prevent meaningful engagement when such input should be essential to this process.

Initial Justification

The written initial offer from CMS, which must be made no later than February 1, 2024, must include a "concise" justification for the offer based on the negotiation factors and the methodology CMS lays out for developing an initial offer. **CMS should describe the template it will use for the concise price justification and, when issuing the initial offer, CMS should discuss the evidence considered, how products met unmet needs, how stakeholders were engaged, the benefits and impacts CMS considered, and mathematical calculations that flow into the price.**

Explanation for the MFP

CMS states that it will publish an explanation for the MFP no later than March 1st of the year prior to the IPAY year. The intent of the published explanation is to summarize how the relevant factors were considered during the price setting process and would focus on the factors that had the greatest influence in determining the MFP. The published explanation will include high-level comments on the submitted data, without any proprietary information. The published explanation will list the selected drug, discuss contributing price setting factors, and note any factors or circumstances that may be unique to the selected drug. If the MFP is not agreed upon, CMS will indicate that no Agreement was reached.

The explanation for the MFP should be released before IPAY 2027 negotiations begin to allow manufacturers to better understand CMS's decision-making process. This is important because, again, the process should be transparent and predictable so that manufacturers (and investors) can incorporate it into their R&D decisions. The explanation should discuss how CMS identified comparators

and therapeutic alternatives for selected drugs, how factors were weighted in CMS' decision-making, evidence sources considered, stakeholders engaged, and benefits and impacts CMS considered.

Average Non-Federal Average Manufacturer Price (Non-FAMP) (Section 60.2.3)

Calculation of Average Non-FAMP

Pfizer recommends that CMS rely upon the existing Veterans Health Care Act (38 U.S. Code § 8126) framework when defining “Average Non-FAMP” values for manufacturer reporting and use in determining MFP. Pfizer strongly opposes CMS’ overly burdensome proposal for a completely new, CMS averaging methodology, relying on quarterly non-FAMP values, to derive unique, “average non-FAMP” calendar year values as the basis for MFP.

In CMS’ proposed guidance, sections 60.2.1, and 60.2.3 with reference to section 50.1, CMS intends to use the non-FAMP of each NDC-11 for the selected drug for each quarter of calendar year 2021 that is submitted to CMS by a manufacturer pursuant to section 1193(a)(4)(A) of the Act, and 1194 (c)(6):

1193(a)(4) ...” (A) information on the non-Federal average manufacturer price (as defined in section 8126(h)(5) of title 38, United States Code) for the drug for the applicable year or period;”

1194 (c)... “(6) AVERAGE NON-FEDERAL AVERAGE MANUFACTURER PRICE. —In this part, the term ‘average non-Federal average manufacturer price’ means the average of the non-Federal average manufacturer price (as defined in section) of title 38, United States Code) for the 4 calendar quarters of the year involved.

In defining the average non-FAMP, the IRA does not specify which four quarters are “the 4 calendar quarters of the year involved” but notably cross-references 38 U.S.C. § 8126(h)(5). To clarify, “the non-FAMP of each NDC-11 for the selected drug for each quarter of calendar year 2021”, should be read as the Annual Non-FAMP value defined in 38 U.S. Code § 8126(h)(5), reported by manufacturers to the Department of Veterans Affairs (VA) by November 15, 2021. Unlike Medicaid Drug Rebate Program quarterly price metrics that determine manufacturer rebate payment amounts for each calendar quarter, only the Annual and Q3 Non-FAMP values are used to determine the Federal Ceiling Price value in effect for the following full calendar year. Therefore, it makes sense to use those same Annual non-FAMP values calculated by manufacturers and reported to the VA by November 15, 2021, as the average annual non-FAMP values for 2021 the IPAY.

Pfizer strongly recommends that CMS revise its approach and adopt Annual Non-FAMPs as the “Average Non-Federal Average Manufacturer Price,” calculated based on four quarters of the federal fiscal year, under VHCA 38 U.S. Code § 8126.

The CMS proposal to “average” four, estimated quarterly non-FAMP values is not used in the VA pricing program. Manufacturers have large volumes of eligible non-FAMP transactions that cross calendar quarters due to the lagged timing necessary for appropriate processing of chargebacks and price adjustments. The purpose of the VA’s annual non-FAMP weighted average calculation methodology is to collect the full data set of all transactions for the applicable 12 months – 4 calendar quarters -10/01 thru 9/30. The overly burdensome, completely new, CMS proposed averaging method, relying on four calendar quarters of quarterly non-FAMP estimated values, which are used only as indicators for pricing trends or, for Q3 Non-FAMPs, as comparators for the FCP additional discount, will result in unreliable

starting values for MFP determination. Manufacturer-reported Annual Non-FAMP values are already subject to VA OIG audit as well as Civil Monetary Penalties for false or late reporting. There is no reasonable basis to not use those values.

CMS Process to Account for Non-FAMP Restatements and Anomalies

The CMS initial guidance does not address the usual processes recognized by the VA as necessary to address situations in which a non-FAMP is restated by the manufacturer or when an anomalous non-FAMP value arises due to a misalignment of sales dollars and units. Manufacturers are able to restate a non-FAMP where the reported non-FAMP is determined to be inaccurate (e.g., sales data flaws, data system problems), or apply VA developed and approved exceptions to address non-FAMP anomalies. Revised Non-FAMP values are not uncommon, and the VA approves adjustments to contract pricing based upon manufacturer restated non-FAMPs and FCPs.

Pfizer recommends CMS adopt MFP calculation exceptions processes to account for Average non-FAMP restatements and anomalies and to clarify how such processes will affect MFP ceiling determination.

Application of the MFP Across Dosage Forms and Strengths (Section 60.5)

In section 60.5 of the Guidance, CMS provides its intended approach to applying a single price across each dosage form and strength of a selected drug in accordance with section 1196(a)(2) of the Act. A key piece of this proposed approach (and indeed, a key piece of the methodologies CMS lays out in sections 60.2.2, 60.2.3, and 60.3 as well) rests on defining 30-day equivalent supplies for each dosage form and strength of a selected drug and therapeutic alternative(s).

CMS should clarify how it will calculate 30-day equivalent supplies, particularly when drugs are used on an as-needed basis and when a 30-day supply cannot provide a reasonable comparison between therapeutic alternative(s). For example, when comparing two products where the treatment duration varies significantly (e.g., an oncology medicine that is administered on an ongoing basis until disease progression vs. a fixed-dose therapy), comparing the cost of a 30-day equivalent supply would not accurately capture the total cost of comparable outcomes. CMS should also give careful thought to how best account for starting dosages of medicines, where a patient's dosage increases over a period of time upon first starting a medication before reaching a steady, long-term dosage amount (i.e., titration). Pfizer and many manufacturers have experience with calculating 30-day equivalent supplies under certain state drug price transparency reporting requirements, and there are certain vendors that assist manufacturers with these calculations. We encourage CMS to discuss with expert stakeholders examples of how 30-day equivalent supplies are calculated for medicines, particularly medicines falling into one of the more complicated situations.

We also request that CMS make available to manufacturers of selected drugs:

- **the Agency's calculated 30-day equivalent supply for each NDC-9;**
- **the total number of units dispensed for each NDC-9 in the 2022 Part D PDE data; and**
- **an Excel template with the Agency's 10-step calculation approach for applying the MFP across different dosage forms and strengths.**

In providing this information to manufacturers of selected drugs, CMS will help to ensure that manufacturers have full transparency into the Agency's calculations.

Dispute Resolution

We are disappointed that CMS does not discuss mechanisms for dispute resolution in the Guidance and urge CMS to establish informal dispute resolution procedures to adjudicate disputes and correct errors in the MFP decision-making process. CMS has significant discretion in establishing informal procedures to resolve disputes and correct errors that will inevitably arise during the MFP decision-making process, and we encourage CMS to exercise this discretion.

Removal from the Selected Drug List (Section 70)

For purposes of a selected drug's exit from the Program, "CMS will consider an approved generic drug or licensed biosimilar biological product to be marketed when [prescription drug event (PDE)] data reveal that the manufacturer of the generic drug or biosimilar biological product has engaged in bona fide marketing of that drug or product." **There is no statutory basis for CMS' proposed "bona fide marketing" standard. Nevertheless, while Pfizer assumes for the purposes of commenting only that CMS's proposed definition of "marketing" is final, Pfizer's view is that CMS' timeline in section 70 for removing a selected drug is overly restrictive.**

Pfizer requests that CMS clarify that the MFP does not apply to a drug that was selected for IPAY 2026 if a generic or biosimilar product is approved and marketed by December 31, 2025. Congress drafted the IRA to enable CMS to set prices for single source products. However, CMS' current position, which is that the agency will continue to set a price for products that become multisource, contradicts Congress' intent and directly undermines generic and biosimilar competition and incentives for pursuing approval of these products.

Manufacturer Compliance and Oversight (Section 90)

Monitoring of Access to the MFP (Section 90.2)

Please refer to our comments on section 40.4 for a discussion of CMS' proposals in section 90.2 of the Guidance.

Monitoring for Bona Fide Marketing of Generic or Biosimilar Product (Section 90.4)

CMS' proposed monitoring of the status of competition in the drug marketplace is unauthorized and unnecessary. There is no statutory basis for CMS' proposal "to monitor whether robust and meaningful competition exists in the market once it makes such a determination [that a generic drug or biosimilar biological product has been marketed]." The Federal Trade Commission (FTC) has the authority and expertise to monitor the status of competition in the drug marketplace. The FDA's Biosimilars Action Plan and Drug Competition Action Plan also supplement the FTC's efforts in addition to joint statements and workshops. CMS should avoid adding another layer of burdensome enforcement.

The statute defines a QSSD in relevant part as a drug for which a generic or biosimilar product is not "marketed." The guidance instead refers to a new term "bona fide marketing," providing that, "[i]n accordance with 1192(c) and (e) of the Act for the purpose of identifying [QSSDs] for [IPAY] 2026, CMS will review PDE data for a given generic drug or biosimilar . . . and will consider a generic drug or biosimilar biological product to be marketed when that data reveal that the manufacturer of that drug or

product has engaged in bona fide marketing of that drug or product.” **While Pfizer assumes for purposes of these comments only that CMS’ proposed definition of “marketing” is final, the statute does not provide CMS a role in monitoring generic and biosimilar competition.**

Civil Monetary Penalties (CMPs) (Section 100)

In section 100 of the Guidance, CMS addresses the civil monetary penalty (CMP) provisions set forth in section 1197 of the SSA (the Program-related CMPs) and briefly describes the “procedures” CMS intends to follow to impose these CMPs on manufacturers.

Notice-and-Comment Rulemaking on Program-Related CMPs

Basic notions of fairness and due process should encourage CMS to complete notice-and-comment rulemaking before imposing Program-related CMPs on manufacturers. Section 1197 of the Social Security Act authorizes the highest CMP amount related to any federal healthcare enforcement regime. The maximum CMP amount set forth in section 1197(a) is equal to 10 times the difference between the price the manufacturer charges and the MFP. The maximum CMP amount set forth in section 1197(c) of \$1 million per day exceeds other “per-day” CMP amounts in the SSA (such as the maximum \$10,000 per day penalty in section 1927(b)(3)(C)(i) for the similar failure of a manufacturer to provide timely information relevant to Medicaid drug rebates).

CMS rulemaking should include clear and detailed procedures CMS intends to use to levy CMPs, the scope of a manufacturer’s CMP liability in regard to the acts and omissions of third parties, and factors CMS will use to determine whether to assess the CMP and the amount of the CMP.

Combined Rulemaking on CMP Procedures

CMS should undergo a single rulemaking process leveraging well-established precedents to implement IRA drug-pricing related CMP procedures. There is overlap between the CMP provisions governing the program, Part B rebatable drugs, and Part D rebatable drugs. As a result, CMS should undertake notice-and-comment rulemaking. CMS should leverage CMP procedures for Medicare Advantage Organizations and prescription drug plans issued by HHS Office of the Inspector General. CMP procedures should include informal mechanisms such as pre-enforcement letters before formal procedures take effect.

Third-Party Non-Compliance

CMS should not levy CMPs on drug manufacturers for third-party non-compliance. The nature of the pharmaceutical supply chain makes it difficult for primary manufacturers to ensure that the MFP is available to MFP-eligible individuals. Additionally, doing so would force manufacturers to assume more legal liability and disrupt the allocation of risk across contractual Agreements among manufacturers and the supply chain. **At a minimum, CMS should issue a non-enforcement policy to ensure primary manufacturers are not levied CMPs following issuance of the final guidance. If primary manufacturers are penalized due to third parties, CMS should weigh that level of culpability to seek lower penalties.**

CMS Explanation of Factors Used in Assessing CMPs

CMS should articulate the factors used when in assessing CMPs through notice-and comment rulemaking. These factors could include:

- the manufacturer’s conduct;
- the degree of the manufacturer’s culpability;
- the extent of the manufacturer’s knowledge of a violation;
- clarity of existing guidance;
- efforts by the manufacturer to obtain guidance from CMS on compliance-related matters;
- good faith efforts to comply with program submission deadlines and requests for extensions;
- and
- the degree to which manufacturers could exercise control over third parties which a manufacturer relied on in satisfying program requirements.

CMS should construe these factors in favor of manufacturers and in a way that would not trigger CMPs.

Threshold for Manufacturer CMP Liability

CMPs that require manufacturers to “act knowingly” should only apply if manufacturers have actual knowledge of the violation. Given the absence of an applicable statutory definition for the term “knowingly,” CMS should define this term based on its plain meaning -- which requires one to act with actual and specific knowledge of a violation.

Part D Formulary Inclusion of Selected Drugs (Section 110)

Price setting will have significant impacts on the structure of Part D and could reduce patient access to medicines. As plans take on more liability through Part D redesign, plans may tighten formularies as a strategy to manage costs. While Part D plans are still held to the protected classes and two drug per class coverage requirements, plans could elect to cover fewer drugs if they’re currently covering more drugs than required. Additionally, plans may also increase their use of exclusive contracts with manufacturers for preferred tier placement -- resulting in significant risk to patients needing some of the most innovative medicines to treat difficult to treat conditions such as cancer and autoimmune conditions. Plans may seek new flexibility from CMS to reform beneficiary protections (e.g., protected class requirements) in response to higher plan liability under Part D redesign. To ensure patients are protected from various plan attempts to offset costs, CMS should (through the formal notice-and-comment rulemaking process) re-examine and update rules around coverage determinations, appeals, and tiering exceptions to ensure patient access. Additionally, CMS should conduct aggressive formulary oversight to guard against growing utilization management or the narrowing of patient treatment options, including exclusion of medicines.

The Medicare drug price setting process implemented by CMS should have as a key goal expanded access to medicines for Medicare beneficiaries – including coverage, access, and affordability that is as good as or better than what is in place today – rather than more restrictions in coverage. CMS’ process for calculating a final MFP should minimize class effects that result in narrower formularies and fewer treatments for patients. To preserve patient access to drugs, CMS should review and update formulary review standards and monitor tiering, cost-sharing, and out-of-pocket exposure decisions. CMS should

also redefine Part D negotiated price to include all manufacturer price concessions, protect current Part D coverage standards, enforce existing formulary requirements and non-discrimination controls, and re-examine and update rules surrounding coverage determinations, appeals, and tiering exceptions.

* * *

Thank you for considering these comments. If you have questions or need additional information, please feel free to contact me at margaret.davis@pfizer.com or 917-678-1316.

Sincerely,

Margaret Davis

Margaret Davis

Senior Director

Corporate Affairs

U.S. Policy and Government Relations

APPENDIX A

Manufacturer Concerns and Suggestions for CMS' Options to Provide Access to the Medicare Part D Maximum Fair Price (MFP)

I. Program Integrity Challenges Associated with Upfront Price Concessions

There are two main approaches manufacturers use to provide access to differential prices for various end customers, such as providers, pharmacies, and health plans. Under the first approach, manufacturers provide access to discounted prices upfront, either through an entity purchasing a medicine at a discounted price directly from the manufacturer, or by an entity purchasing at a discounted price from a wholesaler. In the latter case, the manufacturer then effectuates the discounted price via a chargeback payment to the wholesaler.

Under the second approach, manufacturers provide access to discounted prices retrospectively through a rebate or statutory discount. A key feature of the retrospective approach is that the manufacturer is providing the price concession after a medicine has been dispensed or administered to a patient, enabling the eligibility of the claim for the price concession to be verified.

Both of these approaches work well in different circumstances, largely based on whether a patient's insurance status is a key determinant in how a claim should be processed. The upfront discount approach works well in situations where price concessions are not payer- or patient-dependent. For example, upfront discounts are commonly used by manufacturers to offer price concessions to groups of providers. In this instance, the price concession does not vary by patients' insurance status, but is instead a blanket discount, regardless of the patients the provider group treats. The retrospective approach works well in situations where price concessions do vary based on the payer or patient. For example, retrospective rebates are typically used by manufacturers to offer price concessions to health plans. The post-dispensing or post-administration claim for the rebate enables the manufacturer and the health plan to match eligible claims with the correct rebate amount.

Problems arise when the upfront approach is utilized for discounts that are payer- or patient-dependent, because the eligibility of a claim for a payer- or patient-specific discounted price is generally unknown to the manufacturer at the time the price concession is given. Pharmacies and providers typically serve a mix of patients with different insurance coverage, only some of whom may be eligible for price concessions. In these instances, there are program integrity risks when a unit of medicine is purchased upfront at a discounted price and is then administered or dispensed to a patient who is not eligible for the price concession.

Providers and pharmacies usually track inventory purchased upfront at differential prices by either physically distinguishing or separating it (i.e., a physical inventory model) or by utilizing a virtual inventory tracking system (also known as a replenishment model). Under the physical inventory model, pharmacies or providers maintain a separate or distinguished stock of medicines purchased at discounted prices. When medicines are dispensed to a patient eligible for the discounted price, units are pulled from the separate stock. Under the replenishment model, no separate or distinguished inventories of medicines are maintained. Rather, the pharmacy or provider will track, typically with a computerized system, units

of medicines dispensed to eligible patients. When a certain threshold of units is reached, the pharmacy or provider places an order to replenish that stock at the discounted price.⁵

Despite these inventory management systems, which are complex to manage and can impose a significant burden on providers and pharmacies, there is substantial evidence that diversion is occurring in programs that currently utilize the upfront approach for payer- or patient-specific price concessions. A notable example is the 340B Drug Pricing Program (340B program). The 340B program requires drug manufacturers participating in the Medicaid Drug Rebate Program to provide discounted outpatient drugs to eligible health care entities (known as covered entities or CEs).⁶ CEs often also use outside contract pharmacies to dispense drugs purchased on behalf of CEs through the 340B program. CEs must ensure drugs purchased at 340B prices are only administered or dispensed to individuals who qualify as 340B patients.

Despite the statutory diversion prohibition – which prohibits CEs from reselling or otherwise transferring 340B-discounted drugs to anyone except patients of the CE⁷ – both the HHS Office of Inspector General (OIG) and the Government Accountability Office (GAO) have found significant diversion issues in the 340B program. For example, according to a 2020 GAO report, of the 1,536 340B findings of noncompliance issued by the Health Resources and Services Administration (HRSA) for audits between fiscal years 2012 and 2019, 546 noncompliance findings (over one-third of the total) were related to diversion. This includes 463 noncompliance findings for dispensing 340B drugs to ineligible individuals.⁸

Additional program integrity challenges can arise when the upfront and retrospective approaches to price concessions are mixed. For example, federal law prohibits subjecting drug manufacturers to both a 340B discount and a Medicaid rebate on the same unit of a medicine (a situation known as a duplicate discount).⁹ But because 340B discounts are provided upfront and Medicaid rebates are provided retrospectively, both the GAO and OIG have noted the risk for duplicate discounts.¹⁰ Proper identification of claims subject to 340B pricing is critical for avoiding duplicate discounts, but this transparency does not exist sufficiently for the current 340B program.¹¹

Given the significant risk of diversion demonstrated when payer- or patient-specific price concessions are provided upfront, we strongly urge CMS to utilize a retrospective statutory discount to effectuate the MFP, similar to how CMS utilizes a retrospective discount approach for the Part D CGDP. This would also lessen the burden on pharmacies and Part D plans, which already have extensive experience with the CGDP model, helping to ensure a smooth implementation of the MFP in 2026. The addition of required 340B claims modifiers in Part D and Part B MA for units subject to 340B pricing would help to avoid

⁵ For an overview of the physical inventory model and the replenishment model, as utilized by contract pharmacies in the 340B program, please see: OIG. Memorandum Report: Contract Pharmacy Arrangements in the 340B Program. February 4, 2014. Available at: <https://oig.hhs.gov/oei/reports/oei-05-13-00431.pdf>

⁶ OIG. Memorandum Report: Contract Pharmacy Arrangements in the 340B Program. February 4, 2014. Available at: <https://oig.hhs.gov/oei/reports/oei-05-13-00431.pdf>

⁷ Public Health Service Act (PHSA) § 340B(a)(5)(B).

⁸ Of the remaining 83 diversion noncompliance findings, 76 findings were for failure to ensure proper inventory management of 340B drugs and 7 findings were for systematic errors in software used to determine 340B eligibility. See GAO. Drug Pricing Program: HHS Uses Multiple Mechanisms to Help Ensure Compliance with 340B Requirements. December 2020. Available at: <https://www.gao.gov/assets/gao-21-107.pdf>

⁹ PHSA § 340B(a)(5)(A). See also GAO. 340B Drug Discount Program: Oversight of the Intersection with the Medicaid Drug Rebate Program Needs Improvement. January 2020. Available at: <https://www.gao.gov/assets/gao-20-212.pdf>

¹⁰ OIG. State Efforts to Exclude 340B Drugs from Medicaid Managed Care Rebates. June 2016. Available at: <https://oig.hhs.gov/oei/reports/oei-05-14-00430.pdf>; GAO. 340B Drug Discount Program: Oversight of the Intersection with the Medicaid Drug Rebate Program Needs Improvement. January 2020. Available at: <https://www.gao.gov/assets/gao-20-212.pdf>

¹¹ OIG. State Efforts to Exclude 340B Drugs from Medicaid Managed Care Rebates. June 2016. Available at: <https://oig.hhs.gov/oei/reports/oei-05-14-00430.pdf>

duplicate MFP and 340B discounts as required under the IRA.¹² This is similar to an OIG recommendation to minimize the risk of duplicate 340B discounts and Medicaid rebates.¹³

II. Overview of the Part D Coverage Gap Discount Program

For drugs to be covered under Medicare Part D, manufacturers must provide applicable beneficiaries with access to discounted prices for brand drugs filled in the Part D coverage gap at the POS. The CGDP was created by the passage of the Patient Protection and Affordable Care Act (ACA) in March 2010 and became effective less than nine months later in January 2011.¹⁴ The ACA required CMS to use a TPA to operationalize the CGDP,¹⁵ and Palmetto GBA (Palmetto) has served in this role since the beginning of the program.

The CGDP operates seamlessly at the POS for patients. At the time a pharmacy claim is adjudicated for an eligible Part D enrollee in the coverage gap, the Part D plan (or pharmacy benefit manager (PBM) acting on its behalf) includes the manufacturer coverage gap discount amount as part of the plan's reimbursement to the pharmacy, maintaining a POS patient benefit and ensuring the pharmacy receives full reimbursement on the same schedule as it would otherwise. To cover this additional payment from the Part D plan to the pharmacy on behalf of the manufacturer, CMS provides plans with an additional prospective per member per month (PMPM) payment based on projections in plan bids and plan enrollment.¹⁶

Part D plan payments of coverage gap discounts at the POS are captured on the Prescription Drug Event (PDE) record. Through authority granted by CMS, Palmetto accesses the PDE data and tabulates coverage gap discount liability for each manufacturer. Palmetto then invoices manufacturers on a quarterly basis and provides claims-level data to manufacturers for verification. Manufacturers pay Part D plan sponsors through a direct payment process managed by Palmetto.¹⁷ Part D plan sponsors and CMS then reconcile received manufacturer payments against the prospective PMPM CMS payments at the end of the Part D contract year.¹⁸

The CGDP has a proven track record of providing a POS benefit to patients and is a model well known to CMS, health plans, pharmacies, and manufacturers. This makes the CGDP an ideal model for effectuating the MFP.

III. Effectuating the MFP in Medicare Part D

CMS can operationalize a model similar to the CGDP to offer enrollees the benefit of the MFP at the POS in Part D (see Appendix A). For a discussion of how the MFP statutory discount amount should be defined for the Part D program, please see the “Calculating the MFP Statutory Discount” section later in this paper.

¹² SSA § 1193(d).

¹³ OIG. State Efforts to Exclude 340B Drugs from Medicaid Managed Care Rebates. June 2016. Available at: <https://oig.hhs.gov/oei/reports/oei-05-14-00430.pdf>

¹⁴ SSA § 1860D-14A; Pub. L. No. 111-148, as amended by Pub. L. No. 111-152.

¹⁵ SSA § 1860D-14A(d).

¹⁶ CMS. Medicare Coverage Gap Discount Program Beginning in 2011: Revised Part D Sponsor Guidance and Responses to Summary Public Comments on the Draft Guidance. May 21, 2010. Available at: https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/2011CoverageGapDiscount_Revised-Guidance-052110.pdf

¹⁷ CMS. Coverage Gap Program Technical Guide. Version 1.0. August 2021. Available at: https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/Coverage_Gap_Discount_Program_Technical_Guide_08.2021.v1.pdf

¹⁸ CMS. Medicare Coverage Gap Discount Program Beginning in 2011: Revised Part D Sponsor Guidance and Responses to Summary Public Comments on the Draft Guidance. May 21, 2010. Available at: https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/2011CoverageGapDiscount_Revised-Guidance-052110.pdf

Patient cost sharing at the pharmacy counter for selected drugs dispensed to Part D enrollees would be based on the MFP.¹⁹ Much like the CGDP, Part D plans (or PBMs acting on their behalf) would pay the MFP statutory discount amount to the pharmacy on behalf of drug manufacturers at the time of claim adjudication. This would ensure that the pharmacy receives its full reimbursement on the same schedule as it would otherwise, a crucial protection for independent community pharmacies that may not be able to financially sustain a negative balance on purchased medicines for a prolonged period of time. In addition, this approach builds upon existing direct financial links between Part D plans and pharmacies (whereas manufacturers do not typically have direct financial links to pharmacies). To cover Part D plan liability for paying the MFP statutory discounts on manufacturers' behalf, CMS would include an additional, prospective PMPM payment to Part D plans based on projections in plan bids and plan enrollment.²⁰

The MFP statutory discount payments would be captured on the Part D PDE data record. A TPA would receive access to the PDE for the purpose of tracking and tallying MFP statutory discount liabilities for each drug manufacturer. Manufacturers would be invoiced on a quarterly basis and the MFP TPA would facilitate the distribution of payments to Part D plans.²¹ CMS and Part D plans would then reconcile the PMPM prospective payments against manufacturer payments at the end of the Part D contract year.

This operational approach is highly similar to the current CGDP, making it straightforward and efficient for CMS to implement quickly and ensuring POS availability for Part D enrollees.

Under the CGDP today, manufacturers may access limited claims-level data from Palmetto to help verify that manufacturers are being invoiced for the appropriate amount. We urge CMS to provide similar access to data through the MFP TPA and to continue to allow manufacturers to dispute invoice errors.²²

In addition, we encourage CMS to consider a few key changes under a future MFP statutory discount process. Specifically:

- The data fields made available to manufacturers should be expanded beyond those currently available under the CGDP. A minimum list of data fields that should be made available to manufacturers is included as Appendix B.
- Detailed claims-level data should be made available to manufacturers at the time of invoicing to help manufacturers effectively verify eligible claims and statutory discount amounts. Data included in the invoice and the detailed claims-level data should be made available to manufacturers in a more easily accessible format that does not require external technology to decode, along with an accompanying data dictionary with descriptions of all data fields.
- If a manufacturer files a dispute, the MFP TPA should be transparent and provide clear reasoning and detailed data to support the status of the dispute and resolution. The dispute process should also ideally be shortened relative to the length of the dispute process that can occur under the CGDP today.

¹⁹ The “negotiated price” for a Part D selected drug may not exceed the MFP plus a dispensing fee. SSA § 1860D-2(d)(1)(B)(as amended by the IRA). Long-standing CMS guidance provides that the Part D “negotiated price” is the basis for patient coinsurance and patient payments for a drug in the deductible.

²⁰ CMS should look to SSA § 1196(a)(3) to pre-pay these amounts. We welcome additional discussion with CMS on approaches for the prospective payment of the statutory discount amounts.

²¹ Pub. L. No. 111-148, § 3301(b) prohibited CMS from receiving manufacturer CGDP payments directly, resulting in the structure where manufacturers submit payment to Part D plans who then reconcile with CMS against the prospective PMPM payments. In contrast, the IRA does not prohibit CMS from receiving manufacturer MFP statutory discount payments. Accordingly, CMS could also consider having manufacturers reimburse the Agency directly instead of Part D plans.

²² It is important to recognize that the IRA’s limitation on administrative review does not prohibit CMS from establishing such a dispute resolution process – which would be more akin to reconsideration, as opposed to a formal administrative appeal.

When applied to the IRA MFP process, these minimal changes are expected to result in an improved invoicing, dispute, and appeals process and would not be unduly burdensome to operational stakeholders.

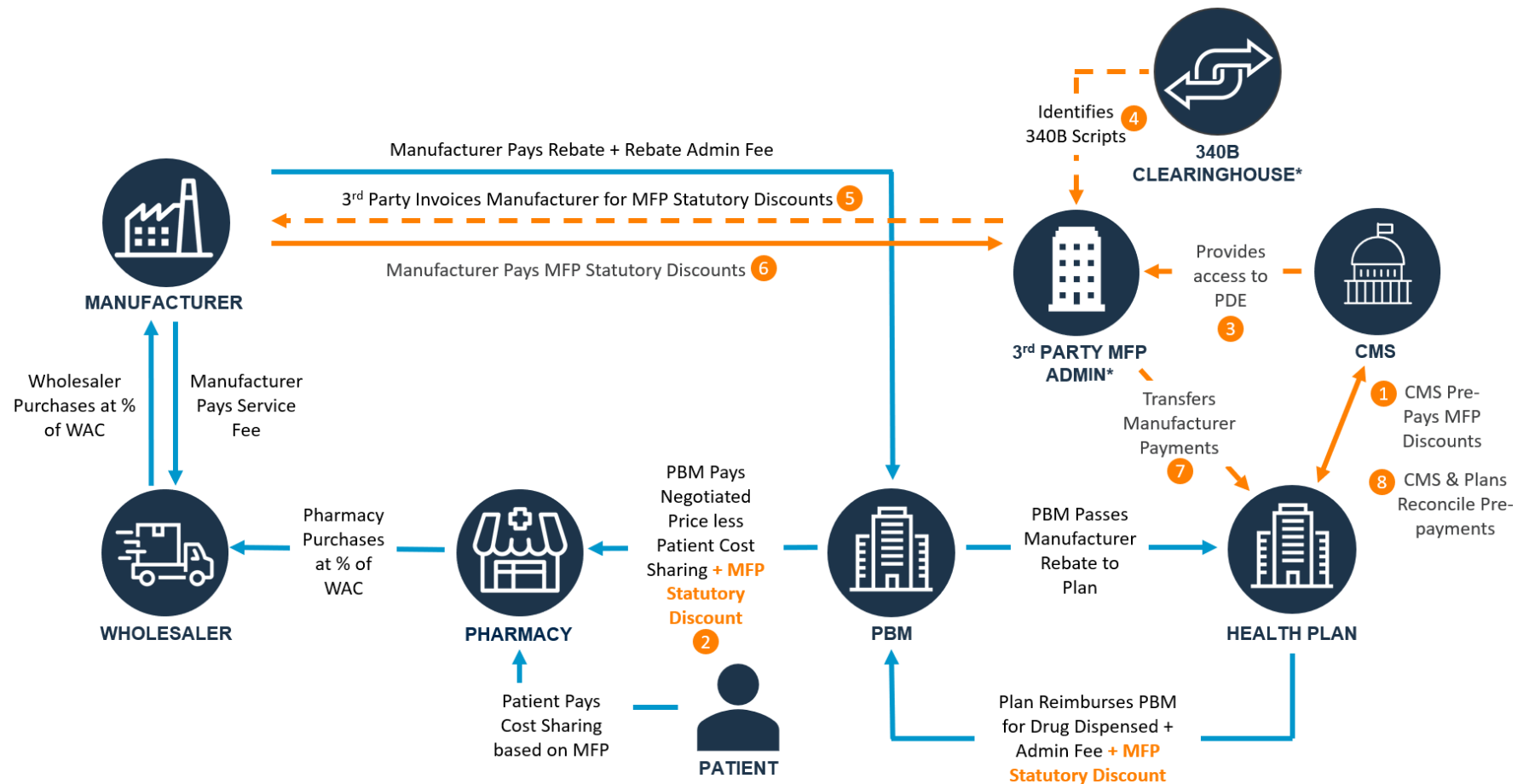
IV. Principles for Selecting an MFP TPA

While there is an array of entities capable of serving as the MFP TPA, we recommend some principles for the Agency to follow in choosing these entities:

- The TPA entity should have demonstrated expertise in working with Part D PDE data, Part B CMS-1500/837P claims, and MA Encounter Data.
- The same entity would ideally be able to serve as TPA across Part D, Part B FFS, and Part B MA to minimize operational differences.
- The TPA entity should be able to serve as the MFP TPA without creating conflicts of interest with existing business lines and without creating the potential for misaligned incentives that may increase costs for patients and the health care system.
- The TPA entity should provide invoices and detailed data to manufacturers for verification in a format that is easy to access and should commit to not utilizing these data (or selling them) for other purposes.
- The TPA entity should be committed to transparency in invoicing and a robust dispute resolution process with manufacturers.
- The TPA entity should meet performance metrics established by CMS, including metrics related to sharing detailed data with manufacturers within the required timeframe.

Appendix B – Effectuating the MFP in Part D with a Third-Party MFP Administrator

This schematic shows a typical operational flow between stakeholders in Part D today and how the operational model for effectuating the MFP as a retrospective discount would factor in. There is some variation in the operational flow today not captured here (for example, not all Part D plans have a PBM operate on their behalf, in which case the Part D plan would reimburse the pharmacy and receive manufacturer rebates directly).



Appendix B – Part D Required Data Fields

In order to verify the calculation of MFP statutory discount amounts owed by the manufacturer, at a minimum the third-party MFP administrator should make the following data fields available to manufacturers on a detailed claims-level basis at the time of invoicing. The majority of these data fields are already available through the PDE record, reducing the burden of sharing these fields with manufacturers. Additional data fields beyond those listed below could be helpful to manufacturers, and we welcome the opportunity to discuss these with the Agency.

- Date of Service (i.e., date filled)*
- Prescription ID Number*
- Part D Contract ID and Part D Plan Benefit Package ID
- De-identified Part D Beneficiary ID
- Prescriber National Provider Identifier (NPI)
- Pharmacy NPI*
- 340B Covered Entity ID/NPI
- National Drug Code (NDC)*
- Days Supply*
- Quantity Dispensed*
- Fill Number*
- Paid Date (date the Part D plan paid the pharmacy)
- Claim Status (whether the claim was paid or reversed)
- 340B Claims Modifier Field
- Clearinghouse Determination of 340B Claim
- 340B Ceiling Price (received from clearinghouse)
- Maximum Fair Price (MFP)
- MFP Statutory Discount Amount (and any supporting fields utilized in calculating the MFP statutory discount amount)

* These fields are already provided to manufacturers as part of the detailed data reports under the CGDP.



April 14, 2023

Submitted via email to: IRAREbateandNegotiation@cms.hhs.gov

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RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear. Dr. Seshamani:

The Pharmaceutical Care Management Association (PCMA) appreciates the opportunity to submit comments on the Centers for Medicare & Medicaid Services' (CMS) initial guidance regarding implementation of sections 11001 and 11002 of the Inflation Reduction Act (IRA), as published on March 15, 2023, which established the Medicare Drug Price Negotiation Program (hereafter referred to as "Negotiation Program") to negotiate prices for certain single source drugs and biological products.¹

PCMA is the national association representing America's pharmacy benefit managers (PBMs), which administer prescription drug plans and operate specialty pharmacies for more than 275 million Americans with health coverage through Fortune 500 companies, health insurers, labor unions, Medicare, Medicaid, the Federal Employees Health Benefits Program, and through the exchanges established by the Affordable Care Act. Our members work closely with plans and issuers to secure lower costs for prescription drugs and achieve better health outcomes.

Our comments on CMS's initial guidance on the Negotiation Program for Initial Price Applicability Year (IPAY) 2026 can be summarized as follows:

- **The Negotiation Program is not intended to disincentivize manufacturers from negotiating price concessions with Part D plans, including price concessions in excess of the maximum fair price (MFP) for selected drugs.** CMS should thus

¹ CMS. "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments." March 15, 2023. Available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

implement the program in a way that does not disrupt or weaken the ability of Part D plans to negotiate price concessions with manufacturers, both for selected drugs and drugs that are not subject to the MFP. CMS should, in its final guidance, clarify this point, and incorporate this broader theme in its implementation of specific aspects of the program, including in its consideration of manufacturer-specific data for purposes of negotiating with a manufacturer of a selected drug and in determining whether a selected drug will be subject to re-negotiation, as well as in the Part D formulary inclusion of selected drugs requirement.

- **PBMs will play a vital role in administering CMS’s Negotiation Program, such as in providing manufacturers with the necessary verification of whether or not a particular claim is for an MFP-eligible individual.** To most efficiently stand up this new program, CMS should consider whether existing frameworks involving PBMs and pharmacies can best facilitate access to MFP for eligible individuals at dispensing entities. For example, the Coverage Gap Discount Program (CGDP) provides a useful model in which PBMs already facilitate access to price concessions at the point-of-sale to make other supply chain actors whole. Its successor—the Manufacturer Discount Program (MDP)—could be built in such a way that the Negotiation Program’s prices are also operationalized through it.

I. Section 30 – Identification of Selected Drugs for Initial Price Applicability Year 2026.

Background: CMS will take an expansive approach to the Negotiation Program by using a broad definition of a “qualifying single source drug” (“QSSD”) to include all dosage forms and strengths of the drug with the same active moiety (or, for biologics, active ingredient) and the same holder of a New Drug Application (NDA) (or, for biologics, a Biologics License Application (BLA)) —inclusive of products that are marketed pursuant to different NDAs/BLAs. In addition, for purposes of counting the seven or 11 years that must elapse to qualify, CMS will use the earliest date of approval of the *initial* application number assigned to the NDA/BLA holder for the active moiety/active ingredient. Furthermore, in the initial guidance, CMS states that to be considered for the IRA’s orphan drug exclusion, a drug or biological product must (1) be designated as a drug for only one rare disease or condition under section 526 of the Federal Food, Drug, and Cosmetic (FD&C) Act; and (2) be approved by the FDA only for one or more indications within such designated rare disease or condition. Notably, to qualify for the orphan drug exclusion, all dosage forms and strengths and different formulations of the QSSD must meet the criteria for exclusion.

Comment: CMS’s approach effectively eliminates the ability of drug manufacturers to “game the system” and keep some products out of the definition of QSSD. As explained in more detail in our comment on Section 110 below, CMS’s broad approach has the potential to capture potentially dozens of different dosage forms, strengths, and routes of administration for a

selected drug, thereby significantly increasing the number of unique marketed products subject to a MFP in a given year. While we endorse and appreciate the intent of this choice, defining QSSD so broadly may have unintended consequences, particularly with respect to the ability of Part D plans and PBMs to effectively manage their formularies and thus preserve access to lower-cost medication options for beneficiaries.

Our primary concern relates to how CMS's broad definition of QSSD will interact with the IRA's Part D formulary requirement to cover "each covered Part D drug that is a selected drug." CMS's broad definition of QSSD could lead to an (incorrect) reading of this provision as requiring Part D plan sponsors to include in their formularies *every dosage form, strength, or formulation* of the selected drug. As explained in more detail below, such an approach would be inconsistent with the current framework of the Part D program, which does not require formularies to include every dosage form, strength or formulation of a drug, even for "protected class drugs." It is also inconsistent with the framework of the IRA, which preserves and promotes the ability of PBMs to negotiate additional price concessions on drugs subject to the MFP. This reading also does not align with the reality of the pharmacy supply chain: today pharmacies do not generally stock each dosage form, strength, and formulation of a product and doing so would require a significant overhaul to inventory management and supply chain agreements. Given the above, PCMA urges CMS to clarify in its final guidance that it will not take such an approach with regard to the IRA's Part D formulary requirement, and that it will instead proceed with an approach consistent with our request outlined in Section 110 below.

Lastly, as currently worded, the proposed QSSD definition could potentially capture differing routes of administration of a selected drug. We are concerned that this approach may inadvertently encompass drugs with significant variation in cost due to the different routes of administration. Moreover, we are concerned about the potential implications for drugs of a selected drug that are covered under Medicare Part B – i.e., injectable or intravenous drugs furnished "incident to" a physician's service – even though Medicare Part B drugs will not be selected for negotiation until 2028. PCMA urges the agency to clarify in final guidance how access to MFP for these situations will be resolved, and that these drugs are outside the scope of the IRA's Part D formulary requirements.

II. Section 40 – Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026.

Background: CMS intends to enter into an Agreement (a "Medicare Drug Price Negotiation Program Agreement") only with the Primary Manufacturer of each selected drug. To the extent that more than one entity meets the statutory definition of a manufacturer for a selected drug for purposes of IPAY 2026, CMS intends to designate the entity that holds the NDA/BLA for the selected drug to be the Primary Manufacturer subject to an Agreement. Pursuant to section 1193(a)(4), CMS intends to include in the Agreement with the Primary Manufacturer several requirements pertaining to Secondary Manufacturers of the selected drug, including reporting a

list of relevant Secondary Manufacturers and collecting and reporting necessary negotiation data elements and information applicable to any Secondary Manufacturer. CMS also intends to hold the Primary Manufacturer responsible for other aspects of the program, such as ensuring that any Secondary Manufacturer makes the MFP available to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers.

Comment: PCMA supports imposing requirements for all various forms of the selected drug on a single Primary Manufacturer, including requirements pertaining to Secondary Manufacturers. This approach centralizes responsibility for compliance with the Negotiation Program’s requirements outlined in the initial guidance and allows CMS to most efficiently operationalize the requirements of the statute, including the statutory requirement to negotiate a single MFP with “the manufacturer” of a selected drug and the requirement that the Primary Manufacturer provide access to the MFP to MFP-eligible individuals.

As we remarked in our comments on the Small Biotech Drug exception, the various ownership and market licensing structures in place in the pharmaceutical market are more complicated than what Congress laid out in the IRA, and what CMS has laid out in guidance thus far. As such, we recommend CMS work through several iterations of assigning Primary Manufacturer status before settling on the NDA/BLA holder as the default.

III. Section 40.4 – Providing Access to the MFP.

Background: CMS proposes to define “providing access to the MFP” as ensuring that the amount paid by the dispensing entity for the selected drug is no greater than the MFP. To accomplish this, CMS proposes to require that Primary Manufacturers provide access to the MFP to dispensers (e.g., pharmacies) in one of two ways: (1) by ensuring the price paid by the dispensing entity is no greater than MFP; or (2) by providing retrospective reimbursement for the difference between the dispensing entity’s acquisition cost and the MFP. Thus, CMS intends to allow access to MFP by dispensers either at the point-of-sale or through the provision of retrospective reimbursement for the difference. Primary Manufacturers would be required to ensure that dispensers (as well as entities such as wholesalers) are reimbursed the difference between their acquisition cost and the MFP within 14 days.

Comment: PCMA does not believe either option proposed by the agency represents an effective approach at providing access to MFP to dispensers. There is currently no existing mechanism in the supply chain that would allow manufacturers to ensure the price paid by the dispensing entity for a drug dispensed to an MFP-eligible individual is no greater than MFP. Furthermore, dispensing entities purchase most drugs from wholesalers or specialty distributors, who themselves are currently under no obligation to comply with the requirement to offer MFP. On the issue of retrospective reimbursement, existing wholesaler and supplier frameworks do

not facilitate payments from manufacturer to the dispensing entity based upon claims payment.² In practice, it is PBMs that play the primary role in processing retrospective reimbursements on behalf of their members.

Given the above, PCMA instead urges CMS to consider as an alternative the Coverage Gap Discount Program (CGDP) in place today. Under the CGDP, Part D plan sponsors and PBMs facilitate manufacturer price concessions at the point-of-sale, while CMS utilizes a third party administrator (TPA) to aggregate Part D data, distribute invoices to manufacturers, reconcile disputes, and reimburse Part D plans for “advancing” access to the manufacturer discount at the point-of-sale. This existing framework for the CGDP, which CMS has indicated will be largely carried over with the transition to the new Manufacturer Discount Program (MDP) in January 2025, is the most effective approach to facilitate access to the MFP at the point-of-sale, and would fulfill the policy goal of ensuring that stakeholders receive the full benefit of the MFP *at the time of dispensing* an MFP-eligible drug, rather than relying on other lengthier and less efficient processes. CMS should leverage the existing system to best operationalize this critical component of providing access to MFP to dispensing entities. Taking this tack, however, does raise a number of operational questions for additional consideration, namely:

- It may require new reporting and documentation requirements for actual pharmacy acquisition costs for selected drugs via an updated National Council for Prescription Drug Programs (NCPDP) telecommunications standard or acceptance of the use of a standard benchmark payment rate for this purpose alone.
- Given the magnitude of the expected price differences, and high volume of applicable claims, plans may need further assurances about repayment by manufacturers, or for CMS to establish a secured fund for this purpose.³

Furthermore, as mentioned above, pursuant to the IRA, CMS will in January of 2025 transition from the CGDP to the new MDP. On this transition, CMS has stated that

in more detail in our comments on the agency’s information collection request related

² The 340B program, for example, is operationalized through wholesaler chargebacks. It is agnostic to ultimate claims payment. All duplicate Medicaid discount and other reconciliation occurs *after the fact* between manufacturers and covered entities. The reconciliation is not made in real-time, and 340B prices are not generally made available to patients at the point-of-sale.

³ See our comments on the MDP agreement, filed April 10, 2023, in which we identified a manufacturer that had declared bankruptcy and was unable to pay its CGDP obligations.

⁴ CMS-10846, Supporting Statement-Part A.



to the IRA's Part D benefit redesign provisions, PCMA also recommends that CMS align the new MDP agreement with its MFP agreement. PCMA believes this approach would allow CMS and Part D plans to administer the Part D program most efficiently on behalf of beneficiaries.

For IPAY 2026, and the second price applicability year of 2027, only Part D drugs will be selected for negotiation. However, some Part D covered drugs can be administered by physicians and covered under Part B instead. We believe CMS needs to account for access to MFP across both benefits, for a drug that is selected on the basis of its spending in one benefit. Providing access to retail and specialty pharmacy drugs under Part B is not common. The need to provide access outside of a drug's normal benefit will generally work in the other direction: Part B drugs administered incident to a physician service can from time-to-time be prescribed and dispensed in a manner that turns them into Part D covered drugs. The process we propose here would be able to handle these situations, too, since they would simply run through the PBM's claims processing system. Similarly, in a Medicare Advantage Prescription Drug (MA-PD) plan that more holistically manages prescription drug benefits across Parts B and D, the claims adjudication system would be able to offer MFP to the appropriate individuals.

The law continues to allow for the payment of dispensing fees for selected drugs, along with the MFP, and dispensing fees will continue to count toward beneficiary cost-sharing calculations. For non-selected drugs, the negotiated price paid to pharmacies today is not mathematically linked to an actual acquisition cost. Instead, these rates are determined by negotiations between pharmacies and Part D plan sponsors, and account for price concessions paid by or owed to pharmacies for contract performance, among other contract terms. Dispensing fees in the Part D program are not a significant source of revenue to pharmacies as they are in other programs, like Medicaid, where reimbursement is set by law to track with acquisition costs more closely. We believe some Part D plans may negotiate higher dispensing fees for selected drugs than for non-selected drugs in their contracts with pharmacies, to reflect pharmacy revenue needs more appropriately. CMS should understand and acknowledge this market dynamic well in advance of plan year 2026 bids and plan benefit package reviews.

IV. Section 50.1 – Manufacturer-Specific Data.

Background: The IRA directs CMS, for purposes of negotiating the MFP of a selected drug, to consider certain "manufacturer-specific data," as the basis for determining its initial offers. These data are required to be reported by the Primary Manufacturer and include: research and development costs; current unit costs of production and distribution; prior federal financial support for novel therapeutic discovery and development; data on pending and approved patent applications; exclusivities recognized by the FDA and FDA applications and approvals; and market data and revenue and sales volume data in the United States. In the initial guidance, CMS states that it intends for the Primary Manufacturer to aggregate data from both the Primary Manufacturer and any Secondary Manufacturer(s).

Comment: As mentioned above, PCMA appreciates CMS’s language regarding placing the onus on the Primary Manufacturer to collect all required data and information. PCMA urges CMS to further clarify in the final guidance that manufacturer-specific data should originate exclusively from manufacturers, and that the agency will not impose any additional reporting requirements on third parties, such as PBMs, as part of the reporting and collection of manufacturer-specific data.

As for the Negotiation Program itself, PCMA is concerned that the agency’s consideration of “market data and revenue,” which CMS proposes to define to include “manufacturer average net unit price to Part D Plan sponsors,” may serve to deter manufacturers of selected drugs from negotiating additional price concessions with Part D plans, thus disrupting the successful, market-based approach that has made the Part D program so successful over the last two decades. As such, PCMA urges CMS to clarify in final guidance that it will administer the Negotiation Program in a way that does not disrupt or create disincentives for manufacturers to negotiate additional rebates or discounts on selected drugs. Furthermore, and as explained in more detail below, CMS should clarify that consideration of this type of manufacturer-specific data will not by itself trigger a future re-negotiation of MFP.

V. Section 50.2 – Evidence About Therapeutic Alternatives for the Selected Drug.

Background: Under the IRA, CMS is required to consider “evidence about therapeutic alternatives” for purposes of negotiating an MFP for the selected drug. The factors on therapeutic alternatives CMS must consider include: the extent to which the selected drug represents a therapeutic advance and the extent to which the selected drug and the therapeutic alternatives address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy. CMS must also consider the FDA-approved prescribing information for the selected drug and therapeutic alternatives, and evidence on the comparative effectiveness of the selected drug and its therapeutic alternatives. In the initial guidance, CMS states that it intends to consider evidence about therapeutic alternatives submitted by members of the public, including manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested parties. CMS also notes that because the IRA prohibits the agency from using comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill, the agency will not consider information submitted that treats extending the life of individuals in these populations as of lower value, such as the use of quality-adjusted life-years (QALYs).

Comment: PCMA generally supports the consideration of therapeutic alternatives as part of this process. Increasing availability of therapeutic alternatives provides benefits to a range of stakeholders, including providing patients with a wider selection of potentially lower-cost treatment options. PBMs are at the forefront of considering therapeutic alternatives through the use of Pharmacy & Therapeutic (P&T) committees to design patient-centric, value-based

formularies. P&T committees are comprised of independent clinical experts that serve an essential function in evaluating clinical evidence on drugs and recommending placement of drugs on formularies. Consistent with the sources CMS states it will use to evaluate therapeutic alternatives in the context of the Negotiation Program, P&T committees also consider relevant information and evidence from across multiple platforms, including current medical literature, HHS-approved compendia, and widely recognized national, evidence-based guidelines when making formulary recommendations. Given the value of therapeutic alternatives in increasing options to lower cost and clinically effective options, PCMA believes it is appropriate for CMS to also consider this factor for purposes of negotiating an MFP for the selected drug. Furthermore, the IRA prohibits the use of information that treats extending the life of individuals who are elderly, disabled, or terminally ill as of lower value. However, PCMA urges CMS to clarify in final guidance that this general prohibition will not apply to, and is not intended to discourage, the ongoing use of non-QALY measures of cost- or clinical effectiveness.

VI. Section 60.3 – Methodology for Developing an Initial Offer.

Background: For the purposes of determining an initial offer, CMS intends to (1) identify therapeutic alternative(s), if any, for the selected drug; (2) use the Part D net price for the therapeutic alternative(s) that is a Part D drug to determine a starting point for developing an initial offer; (3) evaluate the clinical benefit of the selected drug (including compared to its therapeutic alternative(s)) for the purposes of adjusting the starting point using the negotiation factors, resulting in the “preliminary price”; and (4) further adjust the preliminary price by the negotiation factors outlined in the guidance to determine the initial offer price.

Comment: PCMA supports CMS’s approach of using the Part D net price for the therapeutic alternative(s) as the starting point for negotiation for the selected drug. PCMA agrees with CMS that this approach best enables the agency to start developing the initial offer within the context of the cost and clinical benefit of a group of drugs that treat the same disease or condition, and that the “cost of therapeutic alternatives ... is an important factor when considering the overall benefit that a treatment brings to Medicare beneficiaries.”⁵ In cases where there is no identified therapeutic alternative, PCMA supports CMS’s approach of determining the starting point for the initial offer based on the Federal Supply Schedule or “Big Four Agency” pricing.

CMS will identify the price of each therapeutic alternative that is a covered Part D drug by using Part D Prescription Drug Event (PDE) data and detailed Direct and Indirect Remuneration (DIR) report data. PCMA understands the benefit of this approach to collecting information regarding the price of therapeutic alternatives but urges the agency to implement necessary safeguards to ensure it does not publicly share any proprietary information in a way that could harm or undermine competition. We urge caution in relying upon the detailed DIR reports, as well, since

⁵ CMS Initial Guidance, p. 49.

often Part D plans are allocating price concessions across different strengths and package sizes indirectly. PCMA also urges CMS to clarify that this process will not impose any additional reporting burdens or require additional data submissions from plan sponsors or PBMs.

Last, PCMA urges the agency to clarify that once the MFP is set for a selected drug, a manufacturer's decision to negotiate a price lower than MFP with a particular Part D plan sponsor will not prompt a renegotiation in later years. Pursuant to the statute, once an MFP is established for a selected drug, the MFP is only updated by an annual CPI-U adjustment for the relevant 12-month period.⁶ This is the case unless the selected drug is subject to renegotiation,⁷ which is further limited to select circumstances including *material changes* to the manufacturer-specific and comparative-effectiveness negotiation factors.⁸

Even if CMS considers Part D price concessions as part of its review of “market data and revenue” criterion of manufacturer-specific data for purposes of negotiating the MFP, PCMA urges CMS to clarify that a manufacturer's decision to negotiate a price lower than MFP with a particular Part D plan sponsor alone will not suffice to qualify as a “material change” to the manufacturer-specific negotiation factor that would require a selected drug to undergo renegotiation. This clarification is truly critical. Ambiguity regarding the breadth of the potential impact of the “market data and revenue” criterion on renegotiation may deter manufacturers from negotiating with PBMs. PBMs would be less able to negotiate price concessions that are lower than the MFP, ultimately contravening the IRA's mission of lowering prescription drug costs for patients. In the final guidance, we strongly urge CMS to clearly communicate that the decision of a manufacturer of a Selected Drug to negotiate a discount or other price concession in excess of MFP with a payer is not a “material change” to the manufacturer-specific negotiation factor that would require a selected drug to undergo renegotiation.

VII. Section 70 – Removal from the Selected Drug List Before or During Negotiation, or After an MFP is in Effect.

Background: Pursuant to the IRA, a selected drug will cease to be a selected drug and will no longer be subject to the Negotiation Program if CMS determines: (1) the FDA has approved a generic drug under Section 505(j) of the FD&C Act that identifies as its reference listed drug a product that is included in the selected drug, or the FDA has licensed a biosimilar biological product under section 351(k) of the Public Health Service (PHS) Act that identifies as its reference product a product that is included in the selected drug; and (2) the generic drug or biosimilar biological product, as applicable, is marketed pursuant to such approval or licensure. CMS states that the effect and timing of losing selected drug status will depend on when CMS

⁶ See Section 1195(b)(1)(A) of the Social Security Act.

⁷ See Section 1195(b)(1)(B) of the Social Security Act.

⁸ See Section 1194(f)(2) of the Social Security Act.

makes these determinations. CMS will consider an approved generic drug or licensed biosimilar biological product to be marketed when these data reveal that the manufacturer of the generic drug or biosimilar biological product has engaged in “bona fide” marketing of it.

Pursuant to Section 90.4 of the initial guidance, if CMS makes such a determination that a generic drug or biosimilar biological product has been marketed as evidenced by the PDE data, CMS intends to monitor whether robust and meaningful competition exists in the market once it makes such a determination. Examples of monitoring CMS may conduct include whether the generic drug or biosimilar biological product is regularly and consistently available for purchase through the pharmaceutical supply chain, and whether it is available for purchase by community retail pharmacies in sufficient quantities from their wholesale suppliers.

In accordance with section 1192(c)(1) of the Act, a selected drug that is included on the list of selected drugs for an initial price applicability year will remain a selected drug for that year and each subsequent year beginning before the first year that begins at least nine months after the date on which CMS determines the statutory criteria for removal are met.

Comment: PCMA is supportive of a process for removal from the selected drug list that expeditiously removes a drug from negotiation after generic or biosimilar entry. Expedient removal of a selected drug when removal criteria are met is essential to allow Part D plan sponsors and PBMs to fulfill their role of promoting substitution of generics and biosimilars as lowest net cost products, where applicable. Furthermore, to provide greater certainty surrounding when a drug will be removed from the list of selected drugs, PCMA urges CMS to develop a clear and administrable standard for “robust and meaningful” competition from generic or biosimilar entrants, such that only a product that is truly marketed will trigger the removal from the selected drug list. We generally believe that if a new generic or biosimilar product is available to wholesalers and dispensers through common distribution channels, this should qualify as “bona fide” marketing of that drug or product.

VIII. Section 80 – MFP Eligible Individuals.

Background: The IRA defines “maximum fair price eligible individual” to mean, with respect to a selected drug, the following: in the case such drug is dispensed to the individual at a pharmacy, by a mail-order service, or by another dispenser, an individual who is enrolled in a prescription drug plan under Medicare Part D or an MA–PD plan under Medicare Part C (including enrollees in Employer Group Waiver Plans (EGWPs)) if coverage is provided under such plan for such selected drug; and/or in the case such drug is furnished or administered to the individual by a hospital, physician, or other provider of services or supplier, an individual who is enrolled under Medicare Part B, including an individual who is enrolled in an MA plan under Medicare Part C, if payment may be made under Part B for such selected drug.

Comment: PCMA supports this definition of an MFP-eligible individual. Part D plan sponsors and PBMs will play a critical role in providing manufacturers with the necessary verification of whether or not a particular claim is for an MFP-eligible individual. PBMs already perform this important role in other federal programs, particularly in the 340B program for identified 340B claims, where PBMs help prevent diversion by utilizing necessary verification procedures to ensure that drugs purchased with 340B discounts are provided only to eligible patients.

This is just part of the larger role PBMs will play in the Negotiation Program generally. As mentioned above, PCMA urges CMS to adopt an approach in final guidance that explicitly leverages the existing mechanisms PBMs utilize to facilitate access to price concessions (and thus MFP) at the point-of-sale to both MFP-eligible individuals (in the form of cost-sharing reflected the MFP price) and to dispensers, and to administer the existing rebating system to make other supply chain actors whole.

Furthermore, as we identified in Section 40.4 above, CMS also needs to consider how to effectuate access to negotiated Part D covered drugs to MFP-eligible individuals seeking to obtain through their Part B or Part C benefits. Our suggestion to leverage the MDP in the pharmacy transaction space may not work well for medical benefit applications of the MFP for selected drugs. By 2028, CMS will have had to solve this for the Part B provider community in a more formalized manner. In the meantime, we recommend CMS allow flexibility to plans, keeping in mind the 14 days turnaround included in the draft guidance.

IX. Section 110 – Part D Formulary Inclusion of Selected Drugs.

Background: Pursuant to the IRA, CMS intends to require Medicare Part D plans to include in their Part D formularies “each covered Part D drug that is a selected drug” during Contract Year (CY) 2026 and all subsequent years for which the MFP of the selected drug is in effect during the price applicability period.⁹

Notably, however, as mentioned above, CMS is proposing to take an expansive approach with the program by broadly defining a QSSD that can qualify as a selected drug subject to negotiation to include all dosage forms and strengths of the drug with the same active moiety (or, for biologics, active ingredient) and the same holder of an NDA (or, for biologics, a BLA) — inclusive of products that are marketed pursuant to different NDAs/BLAs. In addition, for purposes of counting the seven or 11 years that must elapse to qualify, CMS will use the earliest date of approval of the *initial* FDA application number assigned to the NDA/BLA holder for the active moiety/active ingredient.

⁹ Section 1860D-4(b)(3)(I) of the Social Security Act.

Comment: CMS’s broad approach to defining QSSDs that can be subject to negotiation, paired with the narrow scope of the orphan drug exclusion, may lead to an increased number of unique marketed products subject to MFP in a given year (e.g., more than 10 unique, marketed products may account for the ten selected QSSDs.) Therefore, PCMA urges CMS to clarify in final guidance that it **will not interpret** the Part D formulary requirement to cover “each covered Part D drug that is a selected drug” as requiring Part D plan sponsors to include in their formularies *every dosage form, strength, or formulation* of the selected drug. The practical impact of taking such an approach cannot be overstated, as it could potentially require a plan to include in its formularies dozens of different dosage forms, strengths, and routes of administration for a selected drug. This would severely undermine a plan’s ability to administer and determine the scope of its formulary to ensure low-cost options for its beneficiaries. It would also be inconsistent with the framework of the IRA, which preserves and promotes the ability of PBMs to negotiate additional price concessions on drugs subject to the MFP.

Moreover, this approach is inconsistent with the current framework of the Part D program. Today, Part D formularies must include drug categories and classes that cover disease states, consistent with Part D program requirements, and within each category or class, must include at least two drugs, regardless of the classification system that is utilized by the plan.¹⁰ While CMS guidance requires that plan sponsors include multiple strengths and dosage forms for each covered drug,¹¹ CMS **does not** require formularies to include **every** dosage form, strength, or formulation of the drug (potentially across multiple NDAs/BLAs). Such a policy would fundamentally undermine the market-based negotiation that underlies the Part D program.

Even in the case of “protected class” drugs, which remain subject to a higher standard than selected drugs (to the extent they fall outside of these classes), Part D plans are only required to cover “substantially all” drugs in the named classes. CMS instituted the protected class policy for plan year 2006 “because it was necessary to ensure that Medicare beneficiaries reliant upon these drugs would not be substantially discouraged from enrolling in certain Part D plans, as well as to mitigate the risks and complications associated with an interruption of therapy for these vulnerable populations.”¹² These are not risks beneficiaries will face, for high-spending blockbuster drugs, in 2026. Formulary inclusion policies for selected drugs should not mimic those for protected class drugs (except if a selected drug is in a protected class, of course). CMS has defined “substantially all” to include several notable exceptions, including: multi-source brands of the identical molecular structure; extended release products when the immediate-release product is included; products that have the same active ingredient or moiety;

¹⁰ Section 1860D-4(b)(3)(C) of the Social Security Act.

¹¹ Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Sec. 30.2.1.

¹² Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements, Sec. 30.2.5.

and dosage forms that do not provide a unique route of administration (e.g., tablets and capsules versus tablets and transdermals).¹³ Thus, even for the protected class requirements—a policy implemented to ensure vulnerable populations have continuous access to needed medications—Part D plan sponsors are not required to cover *every dosage form, strength, or formulation* of a particular drug, thus preserving, to an extent, the ability of PBMs to negotiate over formulary placement for drugs that fall under a protected class. It follows that the IRA’s formulary requirement for drugs subject to negotiation should not be interpreted to be on par with or even *more expansive* than CMS’s protected drug class policy intended to maintain access to medications for certain vulnerable patient populations.

Furthermore, requiring Part D plans to include in their formularies every dosage form, strength, or formulation of the selected drug also does not align with the practical realities of the pharmacy supply chain. Pharmacies today do not purchase and maintain significant inventory of all dosage forms and strengths of relevant drugs. Pharmacies instead purchase in large quantities the most common configurations prescribed for the patients they serve, and subsequently order other forms as needed. Requiring every dosage form, strength, or formulation of a selected drug to be on formulary would thus require pharmacies to completely overhaul existing purchasing and inventory practices. It is unlikely Congress intended for the IRA’s Part D formulary requirement to have such a far-reaching effect on other stakeholders in the drug supply chain.

Finally, the underlying statutory language of the IRA indicates that it was not Congress’s intent to require Part D plans to cover on their formularies every dosage form, strength, or formulation of a selected drug. The relevant statutory language simply states that Part D plan sponsors must “include each covered Part D drug that is a selected drug” that is subject to an MFP for the relevant year.¹⁴ There is no language regarding formulary placement of every dosage form, strength, or formulation of the selected drug subject to MFP in the statute. Had Congress intended for such an expansive reading of the Part D formulary requirement, it would have included clarifying language. Given the above, PCMA urges CMS to clarify in final guidance that a plan can be in compliance with the IRA’s formulary requirement so long as one formulation or dosage of a selected drug subject to an MFP is included in the formulary. Furthermore, consistent with CMS’s existing protected class policy, for drugs subject to an MFP that also fall under one of the six protected classes, CMS can clarify that the agency will continue to enforce its “substantially all” formulary requirements as set forth in Chapter 6 of the Medicare Prescription Drug Benefit Manual. This approach best allows PBMs to fulfil their essential role in negotiating price concessions in addition to the established MFP, while maintaining the agency’s expanded protections for protected class drugs.

¹³ *Id.*

¹⁴ Section 1860D-4(b)(3)(1) of the Social Security Act.



PCMA also notes that, notwithstanding the above, there is no language in the IRA indicating that drugs subject to MFP that are included in a plan's Part D formulary must be exempt from utilization management of any kind. As such, in order to provide certainty regarding this important tool used by PBMs to effectively negotiate price concessions and ensure lower-cost drugs for patients, we urge CMS to clarify in final guidance that it will not impose any restrictions on the ability of PBMs to utilize different utilization management tools on drugs subject to MFP that do not fall under one of the six protected classes.

Conclusion

We appreciate the opportunity to comment on the initial guidance for IPAY 2026 regarding implementation of section 11001 and 11002 of the IRA, which established the Medicare Drug Price Negotiation Program to negotiate prices for certain single source drugs and biological products. We hope our suggestions help CMS to implement the Negotiation Program in a way that utilizes, and does not undermine, the existing market-based approach to the Part D program that has allowed Part D plan sponsors and PBMs to successfully negotiate discounts that benefit patients and the program since the inception of the program. We would welcome the opportunity to meet with the agency to discuss these or any other issues relevant to the initial implementation of the Negotiation Program for IPAY 2026. If you have any questions on these suggestions and recommendations, please do not hesitate to contact me directly at tdube@pcmanet.org.

Sincerely,

Tim Dube

Tim Dube
Vice President, Regulatory Affairs



Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

April 13, 2023

Dear Administrator Brooks-LaSure,

I am writing in response to your March 15 Memorandum on Medicare's Drug Price Negotiation Program, which provides initial guidance on the implementation of sections 11001 and 11002 of the Inflation Reduction Act.

The Pharmaceutical Industry Labor-Management Association (PILMA) is a coalition of trade unions and companies in the biopharmaceutical industry that advances unified policy positions on which our trade union and industry members agree. We wish to highlight serious flaws in the Medicare Drug Price Negotiation Program's initial guidance.

PILMA seeks a strong biopharmaceutical industry in order to support abundant, well-paying union jobs across the full range of trades, from highly skilled to unskilled, from lab technicians to construction workers.

The potential impact on union jobs is the reason PILMA is concerned about CMS's initial guidance. The guidance doubles down on shortcomings present within the Inflation Reduction Act itself, laying out policies that will inevitably hamper the growth of the biopharmaceutical industry and its associated jobs. Indeed, PILMA forecasts a contraction in industry jobs as a result of the IRA. Your initial guidance does not address the issue of industry jobs at all, let alone how to lessen the negative impact of the IRA in this regard.

For example, the guidance makes clear the intention of CMS to penalize companies that seek to safeguard additional discoveries they make about a medication after the Food and Drug Administration approves its initial use. As you are aware, industry often explores successful medications for application to different diseases or at treatment stages different from (typically earlier than) those specified in the initial approval. Additional research can also lead to better safety, dosage refinements, and alternative delivery mechanisms that improve convenience for patients. This is a vital part of industry activity and ensures that our healthcare system gets the most out of new medications. It also supports industry jobs.

Unfortunately, the CMS guidance takes no note of this problem within the IRA, nor does it offer a strategy for mitigation. This absence from the guidance will limit research and development investment and the jobs it supports.

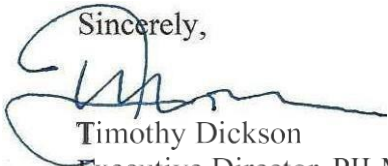
We are also concerned about the disparate jobs impact related to the different exemption periods for price negotiations for small-molecule drugs versus biologics. Your guidance does not address how to assess this differential impact on the workforce.

The guidance, though vague, also makes clear that CMS intends to use a "reference pricing" standard to determine a drug's maximum fair price. At minimum, the reference pricing standard will make it hard to predict what price a developer can expect if its drug works. Given that investments in these drugs need to be made long before they are sure to succeed, the risk of a lower-than-expected determination from CMS affects developers' calculus and investment decisions -- and accordingly, hiring plans and jobs.

Further, your draft guidance appears to impose a kind of "gag order" on biopharmaceutical companies regarding their discussions with and submissions to CMS on participation in price negotiation. We are concerned that the proposed restrictions will lessen the ability of industry executives to be candid with their workers, to the detriment of a close and productive working relationship.

Thank you for considering this comment on the flaws in the Price Negotiation Program's initial guidance. By fixing these shortfalls, CMS can send a message to Americans that it values the workers that make our biopharmaceutical industry the most innovative and productive in the world.

Sincerely,

A handwritten signature in blue ink, appearing to read 'Timothy Dickson', is written over the printed name.

Timothy Dickson
Executive Director, PILMA

April 14, 2023

VIA Electronic Filing – IRAREbateandNegotiation@cms.hhs.gov

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attn: PO Box 8016

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Deputy Administrator Seshamani:

The Pharmaceutical Research and Manufacturers of America (PhRMA) appreciates the opportunity to respond to the Centers for Medicare & Medicaid Services' (CMS, the Agency) *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (Guidance or the Guidance) which was released by CMS on March 15th, 2023.¹ PhRMA represents the country's leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Since 2000, PhRMA member companies have invested more than \$1.1 trillion in the search for new treatments and cures, including \$102.3 billion in 2021 alone.

While PhRMA is pleased to comment on portions of the Guidance, we also have significant concerns about the content of the Guidance, as well as the policies the Guidance implements. The drug pricing provisions of the Inflation Reduction Act (IRA) establish an unprecedented new price-setting authority for medicines in Medicare. This represents a seismic shift from the current market-based systems that underpin both Medicare Part D, which relies on competing plans to control costs, and Medicare Part B, which pays for physician-administered medicines based on discounts available in the market. PhRMA is deeply concerned that this shift will erode patient access and undermine continued biopharmaceutical innovation, particularly progress that occurs after a medicine's initial approval by the U.S. Food and Drug Administration (FDA).

Unfortunately, the Guidance only serves to reinforce and increase our concerns. What the drug pricing provisions of the IRA require is not "negotiation." Unlike negotiations manufacturers enter into with health plans, the Secretary will set prices for selected drugs and enforce them with the threat of legal penalties so severe that no manufacturer could afford to incur them. Given these dynamics, it is imperative that the Guidance establish clear

¹ Available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>

standards and processes to assure stakeholders that CMS' decision making will not be arbitrary and can be influenced by data presented by manufacturers. Unfortunately, the Guidance fails this test. Instead, the Guidance would allow CMS to consider virtually any evidence, and assert that its review of the evidence supports any virtually any decision without any recourse to hold CMS accountable for not following a "consistent methodology", as required by statute.

Indeed, the Guidance describes an approach that fails to give manufacturers and public stakeholders sufficient predictability and transparency. In particular, PhRMA is concerned that the Guidance:

- Provides inadequate (in some cases non-existent) opportunities for meaningful input on the Guidance, as well as the manufacturer "Agreement";
- Establishes requirements as part of the manufacturer Agreement that would undermine the effective implementation of the "Medicare Drug Price Negotiation Program" (the Program), including onerous prohibitions against manufacturers disclosing any information about their experiences under the Program;
- Fails to define a methodology and process for setting "Maximum Fair Prices" (MFP) that are consistent, objective, and predictable; and
- Appears to suggest an approach to determining MFPs that explicitly penalizes innovation.

Specifically, the Guidance implies that CMS is planning to use its discretion to set MFPs using a "cost plus" approach. Suggestions of this approach in the Guidance include statements that CMS "may" use factors such as research and development costs, production and distribution costs, and remaining patents and exclusivities to reduce the price the Secretary would otherwise set for a drug based on the clinical benefits it offers to patients. This approach is wholly incompatible with the economics of the research-based biopharmaceutical sector, in which returns on a small share of commercially successful medicines set investment incentives.^{2,3} Such an approach also devalues therapeutic performance, would be exceptionally destructive to the development of new medicines and indications, and is unnecessary to achieving savings under the law. CMS cites its latitude to determine how or to what degree each factor should be considered. Rather, it should use that latitude to fairly assess the clinical benefit of selected drugs offered to patients and decisively reject a "cost plus" approach.

Compounding problems, the Guidance also falls short of legal requirements, as well as what is widely acknowledged to be a sound policy development process, allowing only 30 days of comment for a program CMS acknowledges is "novel" and "complex."⁴ CMS is incorrect that the Guidance is exempt from procedural requirements of the Medicare statute or the Administrative Procedure Act (APA) and that the Agency need only "voluntarily" accept comments. Under the APA, the Guidance is a legislative rule; under section 1871 of the Social Security Act (SSA), program guidance or program instructions that establish a "substantive legal standard" must be issued with notice and 60 days of comment in the *Federal Register*.⁵ CMS also is wrong to rely on the statutory deadline of September 1st, 2023 as "good cause" to waive notice and comment. CMS waited until

² CBO. (2021). Research and Development in the Pharmaceutical Industry. Available at: <https://www.cbo.gov/publication/57126>.

³ See DiMasi JA, Grabowski HG, Hansen RW, "Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs," *Journal of Health Economics*, vol. 47 (May 2016), p. 25, <https://doi.org/10.1016/j.jhealeco.2016.01.012>.

⁴ 87 Fed. Reg. 62433 (Oct. 14, 2022).

⁵ *Azar v. Allina Health Services*, 139 S. Ct. 1804 (2019). See also HHS Office of the General Counsel, Advisory Opinion 20-05 on Implementing *Allina* (Dec. 3, 2020), https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/2101111604-mh-advisory-opinion-20-05-on-implementing-allina_12.03.2020_signed.pdf. CMS cites to Congress' direction to implement through program instruction or other forms of guidance, but such direction does not explicitly supersede section 1871 or APA requirements. The provision requiring program guidance is not prefaced with a "notwithstanding" clause, a phrasing that would have clarified the IRA's preemptive intent. "Repeals by implication are not favored, and are a rarity." *Maine Cmty. Health Options v. United States*, 140 S. Ct. 1308, 1323 (2020) (cleaned up).

March (approximately seven months after IRA enactment) to publish the Guidance; the fact that the Agency waited longer than it should have to publish guidance does not exempt it from providing required opportunities for stakeholder comment.

We are particularly troubled that the Agency chose to publish a critically important aspect of the Program – “Identification of Selected Drugs for Initial Price Applicability Year 2026” (section 30) – as final, without opportunity for any public input or comment.⁶ The issues addressed in section 30 are extremely important to patients including which drugs and forms would be subject to price setting, the statute’s orphan drug exclusion, and the biosimilars pause. It is a grave error for CMS to adopt the approach outlined in that section without giving stakeholders an opportunity to comment. Manufacturers and PhRMA have expertise in these area and are uniquely positioned to provide CMS with the type of feedback needed on foundational decisions such as the definition of a “qualifying single source drug” (QSSD) and the biosimilar pause. Providers, pharmacies, patients, and their caregivers also provide perspectives CMS should consider in a novel and complex program that sets prices and new reimbursement rates for medicines in Medicare. Finalizing section 30 without notice and comment denies the Agency the expertise of all stakeholders and raises serious legal questions under section 1871 of the SSA and the Due Process Clause of the U.S. Constitution. The approach outlined in section 30 will have far-reaching consequences for PhRMA members and for patients. Most critically, it will shape how innovative biopharmaceutical companies allocate scarce resources as they develop the next generation of treatments and cures, which will be used by patients both inside and outside of the Medicare program. PhRMA notes CMS’ statement that it “may make changes to any policies, including policies on which CMS has not expressly solicited comment, based on the Agency’s further consideration of the relevant issues.” We urge the Agency to reconsider this position and engage on these important matters in the future.

Despite these significant concerns with the Guidance, PhRMA recognizes that CMS has a statutory obligation to implement the Program. Our comments outline recommendations the Guidance can mitigate the harm to patient access and innovation over time. Below we summarize those recommendations for CMS.

REQUIREMENTS FOR MANUFACTURERS OF SELECTED DRUGS (Section 40)

- Abandon the Primary/Secondary manufacturer definition and instead enter into separate Agreements with each manufacturer, as anticipated by the statute.
- Allow manufacturers enough time to comment on the Agreement language before the Agreement deadline; avoid use of open-ended language in the Agreement.
- Open the “confidentiality policy” for public comment and ensure the policy and protocols offer robust protection and security of proprietary information, as outlined in comments below. Abandon the proposed data use limitation as it violates the First Amendment, conflicts with government transparency principles, and cannot be finalized.
- Establish a process to effectuate the MFP for eligible patients that provides manufacturers with access to needed data from the Part D Prescription Drug Event (PDE) records in order to verify that the patient is an MFP-eligible individual.
- Work in coordination with the Health Resources and Services Administration (HRSA) to revise the Guidance to prevent duplicated MFP and 340B discounts as required under the IRA.

⁶ There is an extremely narrow exception for the Small Biotech Exception Information Collection Request (ICR).

NEGOTIATION FACTORS (Section 50)

- Use – and allow manufacturers to submit data from – the FDA’s Orange and Purple Book listings and Drugs@FDA for relevant patent information.
- Allow manufacturers to voluntarily provide additional data, as manufacturers need discretion due to the varied ways in which they record and maintain data on these factors.
- Amend the Information Collection Request (ICR) guidance to allow manufacturers to note where they have provided requested data and ensure that there is sufficient space for companies to provide rationale and references for approximate data calculations.
- Place minimal weight on recoupment of research and development (R&D) costs, and specify that this factor will not be used to reduce an MFP; count only a fraction of global net revenue toward “recoupment” of R&D costs.
- Amend the Guidance to limit required submission of R&D costs to data available to the manufacturer that can be directly attributable to the selected drug, while allowing companies to voluntarily provide supplemental data and a supportive narrative.
- Allow manufacturers to rely on benchmark or industry-wide data in cases where a company may not maintain the data.
- Remove the tax credits from the definition of “prior federal financial support” and limit consideration to funding that resulted in a patent application containing a Government Interest Statement and/or research where a patent assignee was a U.S. government agency for an invention directly related to the development of the selected drug (e.g., excluding basic science, research tools, or similar general concepts).
- Reverse the proposal that penalizes manufacturers for having patents and exclusivities by instead increasing the preliminary price to reflect the innovation in the product.
- Explicitly acknowledge statutory prohibitions against the use of quality-adjusted life years (QALYs) and similar metrics, in any context based on both the language in the IRA and the SSA.
- Require that entities attest to removing all QALY-based research from their data submissions to CMS, including research where the findings were intrinsically influenced by the use of QALYs.
- Develop robust literature review and research standards for the Agency and all external organizations CMS works with on evidence synthesis and technology assessment, both formally and informally, to ensure that the evidence it relies upon or develops is methodologically rigorous and patient-centered.

NEGOTIATION PROCESS (Section 60)

- Set MFPs for selected drugs at or near the ceiling price for all Medicare Part B and Part D medicines beginning with the first several “initial price applicability years” (IPAY) in view of the short timeline for implementation and novelty of the Program.
- In subsequent years, consider setting the MFP for “selected drugs” at the ceiling price in the following circumstances:
 - Selected drugs for which the IPAY is less than 13 years since the medicine’s initial FDA approval, to mitigate consequences of the Program for small molecule medicines;

- Selected drugs for which the statutory ceiling price is the net price, reflecting significant discounts through brand-to-brand competition;
 - Selected drugs that meet or have met the FDA’s definition of unmet need, evaluated across a product’s lifecycle;
 - Selected drugs that meet or have met the New Technology Add-On Payment’s (NTAP) definition of “substantial clinical improvement”, and therefore represent a significant therapeutic advance; and
 - Any selected oncology drug that receives a Category 1 or 2A rating in the National Comprehensive Cancer Network’s Drugs and Biologics Compendium, and therefore represents a significant therapeutic advance.
- Prior to making its initial offer to the manufacturer, CMS should publish and solicit public comment on key elements of its MFP analysis including, but not limited to: 1) therapeutic alternative(s) CMS has identified for any selected drug it is considering (for each indication); 2) data and analysis CMS developed and considered supporting each factor, including evidence provided by third parties engaged formally or informally by CMS; 3) benefits and impacts of a selected drug CMS intends to consider; and 4) stakeholders, and other government agencies and organizations CMS intends to engage, formally or informally.
 - Place a greater weight on the factors related to the benefits that medicines actually offer to patients, caregivers, and society as specified in section 1194(e)(2).
 - Engage relevant experts – including manufacturers and clinicians – as the primary resources for determining therapeutic alternative(s) and provide an opportunity for feedback on therapeutic alternative(s) before the initial offer is made.
 - Use “clinically appropriate” as the standard for decision-making as to a selected drug’s therapeutic alternative or comparator; do not rely on cost to select “therapeutic alternative(s)” and comparators.
 - Consider a comprehensive range of clinical and non-clinical benefits and impacts of a selected drug, including those that are important to patients, caregivers, and society, based on feedback from those stakeholders. Include in the explanation a detailed account of how CMS identified relevant benefits and impacts of a selected drug, data and analysis on each benefit and impact for the selected drug, and how each contributed to the selected drug’s MFP.
 - Provide manufacturers of selected drugs the opportunity to meet with Agency staff at least three times in-person prior to the manufacturer’s counteroffer: 1) after drug selection but prior to initiation of the price-setting process; 2) prior to CMS presenting the initial offer; and 3) after CMS presents the initial offer.
 - Use the annual non-Federal average manufacturer price (non-FAMP) already in use by the U.S. Department of Veterans Affairs (VA), as defined in 38 U.S.C. § 8126(h)(5), in MFP calculations.
 - Describe the template that will be used for the initial, concise justification and ensure it includes: 1) how therapeutic alternative(s) for each indication were selected; 2) how each factor was weighed; 3) data and analysis CMS developed and considered supporting each factor, including evidence provided by third parties engaged formally or informally by CMS; 4) benefits and impacts considered; and 5) stakeholders, and other government agencies and organizations CMS engaged, formally or informally, in the process and how their input factored into the Agency’s offer.
 - Publish the required IPAY 2026 explanation for the MFP before the IPAY 2027 price setting process begins and ensure that all explanations include, at a minimum: 1) therapeutic alternative(s) for each indication and how they were selected; 2) how each factor was weighed; 3) data and analysis CMS developed and

considered supporting each factor, including evidence provided by third parties engaged formally or informally by CMS; 4) benefits and impacts considered; and 5) stakeholders, and other government agencies and organizations CMS engaged, formally or informally, in the process and how their input factored into the Agency's decision-making.

CIVIL MONETARY PENALTIES (CMPs) (Section 100)

- Complete notice-and-comment rulemaking on Program-related CMPs before seeking to impose any such CMPs on manufacturers.
- Implement procedures governing IRA drug pricing-related CMPs through a single rulemaking and model such procedures after well-established precedents.
- Do not impose CMPs on drug manufacturers for acts and omissions of third parties (e.g., secondary manufacturers, dispensers, providers, supply chain intermediaries) over which manufacturers have little, if any, control.
- Clearly explain, through notice-and-comment rulemaking, the factors CMS will consider in assessing whether to seek a Program-related CMP and the amount of any such CMP, and, during the early years of the Program, construe these factors liberally in favor of manufacturers in a manner that would not trigger a CMP.

PART D FORMULARY INCLUSION OF SELECTED DRUGS (Section 110)

- Minimize effects within therapeutic classes that would result in narrower formularies and fewer choices for patients.
- Review and update Part D formulary standards. Monitor plan coverage and tiering decisions, cost-sharing levels, and patient out-of-pocket exposure.
- Redefine Part D "negotiated price" to consider all manufacturer price concessions. Conduct strong oversight of formulary requirements and guard against non-discrimination violations.
- Re-examine and update rules around Part D coverage determinations, appeals, and tiering exceptions.

Our detailed comments follow below.

* * * *

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Introduction

The Pharmaceutical Research and Manufacturers of America (PhRMA) believes that the “Medicare Drug Price Negotiation Program” (the Program), as codified in statute, will have significant consequences that will harm patients and continued biopharmaceutical innovation. In this regard, we are exceedingly disappointed that the Centers for Medicare & Medicaid Services’ (CMS, the Agency) did not take steps in the *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (Guidance or the Guidance)⁷ to mitigate against the law’s negative consequences. We urge the Agency to make changes to address this in revised Guidance.

As CMS revises the Guidance document, and implements the Program broadly, we urge the Agency to consider our recommendations to mitigate against harmful consequences for patients. We also strongly encourage CMS to continuously monitor and evaluate the impact of its policies on patient access to all medicines, including but not limited to selected drugs, and biopharmaceutical innovation, including innovation across a medicine’s lifecycle. Below we describe concerns with government price setting in general before addressing the specific provisions of the Guidance.

The Impact of Price Setting on Patient Access and Biopharmaceutical Innovation

PhRMA is deeply concerned that setting prices for medicines will erode patient access and undermine continued biopharmaceutical innovation. Although national government price setting for medicines is novel for the U.S., it is not for other countries. Experience in these countries illustrates the degree to which government price setting erodes biopharmaceutical innovation and curtails patient access to treatments. Indeed, access delays and barriers are defining characteristics of such foreign systems, which prioritize cost-cutting over access, quality, and innovation. As a result, in countries that set prices for medicines, many patients – including those with cancer, diabetes, autoimmune, and rare diseases – face significant restrictions on access to treatments. Although the Inflation Reduction Act (IRA) differs from the price setting systems in these countries in several fundamental ways, the potential harm to patient access remains in any system in which the government is making a policy judgment related to a health intervention’s benefits and costs at a national level.

Data on the availability of medicines in foreign countries underscores the challenges patients face as a result of price setting. For example, 85 percent of all new medicines launched between 2012 and 2021 are reimbursed in Medicare/Medicaid programs, compared to other countries’ public health care programs where only 61 percent of new medicines are reimbursed in Germany, 48 percent in the United Kingdom, 48 percent in Japan, 43 percent in France, 24 percent in Australia, and 21 percent in Canada.⁸ In these countries, it takes an average of 27 months longer than in the U.S. for new medicines to become reimbursed by a public plan.⁹ The statistics underscore the importance of CMS implementing the Program in ways that help mitigate these potentially devastating effects.

In addition to potential harms to patient access for currently available treatments, government price-setting programs will invariably undermine incentives for biopharmaceutical innovation in the U.S. As a result of a health care system that relies on the strengths of market competition to balance cost control, patient access, and continued innovation, the U.S. leads the world in both research and development (R&D) for lifesaving treatments and cures. However, this was not always the case. In 1990, biopharmaceutical R&D investment in Europe was

⁷ Available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

⁸ PhRMA analysis of IQVIA MIDAS and country regulatory data, October 2022. Note: New active substances approved by FDA, EMA and/or PMDA and first launched in any country between January 1, 2012, and December 31, 2021. A medicine is considered publicly reimbursed in Canada if 50 percent or more of the population lives in a province where it is reimbursed by the public plan. A medicine is considered publicly reimbursed in the United Kingdom if recommended by England’s National Institute for Health and Care Excellence (NICE) for funding by England’s National Health Services (NHS).

⁹ PhRMA analysis of IQVIA Analytics (2023).

more than 45 percent higher than similar investment in the U.S. However, decades of implementation of price controls and other anti-innovation policies across Europe pushed the locus of industry to the U.S., and as a result, reversed that dynamic.¹⁰ In 2004, the U.S. Department of Commerce found that price controls in certain Organisation for Economic Co-operation and Development (OECD) countries suppress investment in worldwide R&D by 11 to 16 percent annually, which leads to fewer new medications being launched each year.¹¹ These effects likely have grown worse in the two decades since this research was published.

The IRA's drug price-setting provisions are already having an impact on biopharmaceutical R&D decisions. In the months following IRA passage, several biopharmaceutical manufacturers have announced cancellations of pipeline projects as a direct result of the law. A 2022 survey of PhRMA member company leaders shows that a majority have concerns – three-quarters of leaders responding to the survey said the IRA creates significant uncertainties for R&D planning and that they already are reconsidering R&D investment strategies, and 78 percent reported that early-stage pipeline projects are likely to be cancelled due to IRA provisions.¹² Fewer products in early-stage development will lead to fewer new cures and treatments for patients in the long run. Small molecule medicines, such as medicines for cancer that come in pill or tablet form, are particularly vulnerable to losing out on R&D investments, due to the short timeframe under which they can become eligible for price setting.¹³ In the recent survey, 63 percent of respondents said they expect to shift R&D investment away from small molecule medicines.

While the price-setting framework in the IRA poses a threat to all biopharmaceutical innovation, it is particularly harmful to the R&D that occurs after a medicine's initial U.S. Food and Drug Administration (FDA) approval in the years leading up to and after a drug becomes eligible for price setting. In the aforementioned 2022 survey, 95 percent of respondents stated that they expect to develop fewer new uses for medicines due to the limited time available before a drug is subject to government price setting. The methodology for price setting should, to the extent possible, consider and preserve the intent of the intellectual property protections provided for companies to invest in biopharmaceutical R&D as well as the incentives for R&D that takes place after the initial FDA approval, including ongoing research that identifies important new uses of existing drugs.

There are numerous examples of medicines that have conferred benefit after their initial FDA approval. For example, an infused cancer drug originally approved via the accelerated approval pathway in 2014 to treat advanced or unresectable metastatic melanoma has since been approved for more than 35 different indications across 16 tumor types. This includes a recent FDA approval on January 26th, 2023 for adjuvant treatment following resection and platinum-based chemotherapy for stage IB, II, or IIIA non-small cell lung cancer (NSCLC).¹⁴ This is the type of research and innovation CMS' implementation puts at risk.

Recent research further underscores the frequency at which post-approval innovation occurs. The Partnership for Health Analytic Research studied the development of improvements to medicines that received initial FDA approval between 2010 and 2012. Of these 88 medicines, more than half were later approved by the FDA for at least one additional indication. For cancer, the share was even higher; 62 percent of oncology medicines were

¹⁰ Moll, N. (2020). Would the last pharmaceutical investor in Europe please turn the lights out. European Federation of Pharmaceutical Industries and Associations. Available at: <https://www.efpia.eu/news-events/the-efpia-view/blog-articles/would-the-last-pharmaceutical-investor-in-europe-please-turn-the-lights-out/>.

¹¹ U.S. Department of Commerce. (2004). Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation. National Technical Information Service.

¹² Longo, N. (2023). WTAS: Inflation Reduction Act already impacting R&D decisions. PhRMA. Available at: <https://catalyst.phrma.org/wtas-inflation-reduction-act-already-impacting-rd-decisions>.

¹³ Powaleny, A. (2023). IRA Impacts: Cancer treatment research and development. PhRMA. Available at: <https://catalyst.phrma.org/ira-impacts-cancer-treatment-research-and-development>.

¹⁴ Keytruda [package insert]. Whitehouse Station, NJ: Merck & Co., Inc; 2023. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125514s1281bl.pdf.

later approved for one or more additional indications, a majority of which were approved seven or more years after approval.¹⁵ Since the IRA creates disincentives for investment in indications post-original FDA approval, we suggest CMS give appropriate weight to post-approval innovations that deliver significant clinical benefit to patients, caregivers and society when determining Maximum Fair Prices (MFP) for selected drugs. In some instances, products with a number of indications that offer such significant benefit should be priced at or near the statutory ceiling.

PhRMA is also concerned about the potential impact of the IRA on orphan drug development, which often includes R&D on medicines for a rare disease that also might provide promise for non-orphan diseases with a related causal pathway. PhRMA notes that CMS has issued section 30.1.1 and its approach to determining eligibility for orphan drug exclusion in that subsection as final without accepting comments. Accordingly, as with the remainder of section 30, PhRMA is not commenting on the approach outlined in that subsection. PhRMA nevertheless notes CMS' statement that it "is considering whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development." PhRMA looks forward to engaging with CMS on this issue outside of the context of this Guidance process and encourages the Agency to issue guidance as expeditiously as possible, with appropriate opportunity for and consideration of public comment, on this important subject.

The aforementioned dangers to patient access to current and future treatments reinforce that CMS should design its methodology to mitigate negative effects on patients and continued innovation. CMS' MFP methodology should also reflect the reality that Part D sponsors already receive significant rebates on many drugs likely to be selected, and that the ceiling price set in statute can represent an additional deep discount to the Medicare program for these medicines.¹⁶ Given the previously discussed consequences of price setting, CMS should be cautious when setting MFPs below the statutorily defined ceiling price. Setting prices for medicines is a highly complicated and technical undertaking that CMS must complete on an exceedingly short timeline and with limited existing expertise to build upon.¹⁷ Challenges facing the Agency in this regard have also been acknowledged by CMS officials themselves, who have noted that the timelines are "tremendously tight for us."¹⁸

While we appreciate CMS taking the important step of issuing a Guidance, we note that it was published only five and a half months before the Agency is required to publish its list of ten selected drugs on September 1st, and only six and a half months before signed "Agreements" and complex, voluminous data submissions will be due from manufacturers. As a result, given these delays, we believe it is important for CMS to recognize the reality that neither the Agency nor manufacturers have a realistic period of time to prepare for implementation. In light of this, as described in more detail below, we believe CMS should commit to setting final MFPs at or near the deep, statutorily mandated "ceiling price" discounts in the first several years of the Program.

PhRMA also recommends that, consistent with longstanding principles of administrative law and good guidance, CMS respond in writing to comments on the Guidance, and that CMS maintain a public docket of comments received. Further, consistent with the timetable announced by CMS, we support completion and publication of

¹⁵ Ortendahl, J. D., Lee, J. S. (2022). Implications of the Inflation Reduction Act on Post-Approval R&D of Biopharmaceutical Medicines. Partnership for Health Analytic Research. Available at: <https://www.pharllc.com/wp-content/uploads/2022/11/Clinical-Benefits-of-Post-Authorization-Research-Brief.pdf>.

¹⁶ CBO. (2021). A Comparison of Brand-Name Drug Prices Among Selected Federal Programs. Available at: <https://www.cbo.gov/system/files/2021-02/56978-Drug-Prices.pdf>; CBO (2023) How CBO Estimated the Budgetary Impact of Key Provisions in the 2022 Reconciliation Act. Available at: <https://www.cbo.gov/system/files/2023-02/58850-IRA-Drug-Provs.pdf>.

¹⁷ As just one example, the Guidance states CMS will use a "qualitative" approach to consider on an indication-by-indication basis "nuanced differences between different drugs" on numerous dimensions of clinical performance, for a range of specific subpopulations. (Sections 50.2, 60.3.1, 60.3.3.1) CMS does not have a significant experience in performing and has not demonstrated its capability to perform such assessments. Moreover, this is only one of many novel areas for CMS that are part of price setting.

¹⁸ Kelly, C. (2023). Medicare Price Negotiation: Data Needed to Establish 'Unintended Consequences' – CMS' Blum. Pink Sheet. Available at: <https://pink.pharmaintelligence.informa.com/PS147732/Medicare-Price-Negotiation-Data-Needed-To-Establish-Unintended-Consequences--CMS-Blum?vid=Pharma&processId=0ad1a798-00c5-4c4b-b635-ace165a12f44>.

Guidance with at least two months' lead time before the first list of selected drugs is announced on September 1st, 2023. We appreciate the Agency's reaffirmation in an April 7th communication that it plans to publish revised Guidance this summer, as well as its commitment to publicly posting the comments it receives.¹⁹ In addition, we request to see the Agreement in advance of CMS' selection of drugs for price setting to give manufacturers opportunity to comment and time to review the Agreement in order to enter the price setting process.

Some of the flaws in the initial guidance appear to reflect a misperception that the Program represents a "negotiation" akin to manufacturer negotiations with health insurance companies. In fact, it is very different. Regardless of the term being used in statute, the Program is a federal policy decision-making exercise that involves both a non-public component (manufacturer submission of proprietary data and CMS communication directly with the company) and a public component (e.g., public solicitation of input to inform the Agency's decision and public explanation of the decision).

PhRMA's comments on specific provisions in the Guidance are set forth below. The recommendations are driven by our expertise on many of the issues on which CMS seeks comment and are offered to help mitigate against unintended and negative consequences to patients and innovation. We urge CMS to revise its Guidance in response to the below recommendations.

* * * *

I. Requirements for Manufacturers of Selected Drugs (Section 40)

Section 40 of the Guidance focuses on the "Agreement" that manufacturers must enter with CMS under the Program and other issues related to the Agreement. PhRMA is concerned that several provisions in this section exceed CMS' statutory authority, are unworkable, and contribute to a decision-making framework that is subjective and unpredictable. We describe these concerns, and recommend modifications, in more detail below.

a. Primary/Secondary Manufacturer Definition

CMS' proposal to establish separate categories of "Primary" and "Secondary" manufacturers, and to hold Primary Manufacturers responsible for other distinct corporate entities ("Secondary" manufacturers), is unworkable and not supported by statute. In section 40, CMS notes that the IRA adopts the definition of "manufacturer" in section 1847A(c)(6)(A) of the Social Security Act (SSA) (which derives from the Medicaid rebate statute).²⁰ CMS then explains that the IRA directs it to negotiate an MFP with "the manufacturer" of a selected drug.²¹ If "more than one entity meets the statutory definition of manufacturer for a selected drug for purposes of [initial price applicability year (IPAY)] 2026," CMS states, it "intends to designate the entity that holds the [New Drug Application(s) (NDA(s)) / Biologic License Application(s) (BLA(s))] for the selected drug to be 'the manufacturer' of the selected drug (hereinafter 'Primary Manufacturer')." Any other entity that meets the statutory definition of manufacturer for a drug product included in the selected drug and "either (1) is listed as a manufacturer in an NDA or BLA for the selected drug or (2) markets the selected drug pursuant to an Agreement with the Primary Manufacturer" would be deemed a "Secondary Manufacturer." Secondary Manufacturers would include any manufacturer of any authorized generics and any repackager or relabeler of the selected drug that "meet these criteria."

CMS proposes to sign an Agreement only with the Primary Manufacturer, under which CMS states that the Primary Manufacturer would be required to agree, among other things, to:

¹⁹ Centers for Medicare & Medicaid Services. (Email announcement, received April 7, 2023). Medicare Drug Price Negotiation Initial Guidance: Comments due by April 14.

²⁰ SSA § 1191(c)(1), incorporating 1847A(c)(6)(A), incorporating § 1927(k)(5).

²¹ SSA § 1193(a)(1).

- Report manufacturer-specific information applicable to any Secondary Manufacturer (and in some cases to blend pricing data of the Secondary Manufacturer with its own pricing data);²²
- Ensure that any Secondary Manufacturer(s) make the MFP available to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers;
- Respond to CMS requests within “specified timeframes” with documentation demonstrating compliance and remedial actions, as applicable, pursuant to reports of noncompliance or other CMS compliance and oversight activities; and
- Pay any CMPs for violations (including those stemming from noncompliance by any Secondary Manufacturer).

Other than citing to use of the word “the,” CMS cites to no other statutory authority for imposing vicarious liability on Primary Manufacturers. And the provision immediately preceding the paragraph referencing “the manufacturer” mentions multiple Agreements with multiple manufacturers, stating that the “Secretary shall enter into Agreements with manufacturers of selected drugs.”²³ The reference to “the” manufacturer, thus, merely refers back to each Agreement CMS maintains with each of the various manufacturers signing these Agreements. If more than one legally distinct entity meets the definition of “manufacturer,” then CMS may enter into separate Agreements with each of such manufacturers, and there would be one “manufacturer” or “the manufacturer” under each Agreement. As a result, Congress’ use of “the” hardly merits the significance CMS reads into it, and certainly does not warrant adopting a policy that conflicts with ordinary corporate responsibilities.²⁴

Nothing in the IRA authorizes CMS to impose requirements, liability, or certainly not excise taxes, on a legal actor who maintains a distinct corporate identity. While CMS may argue that the IRA permits adding requirements “determined by the Secretary to be necessary for purposes of administering the program and monitoring compliance with the program,”²⁵ CMS’ proposal goes beyond anything “necessary” to administer the MFP program. In fact, CMS arguably could monitor a manufacturer’s compliance more easily if it maintains an Agreement with each distinct corporate entity – such that it is directly, rather than indirectly, holding each entity accountable.

Any other reading of the language would amount to Congress delegating to CMS major corporate law questions of holding one entity responsible for the activities of an unrelated corporate actor, even though there is no indication in the IRA that Congress intended to grant the Secretary powers so extensive as to alter ordinary laws of corporate liability, or to require amendments to the contracts Primary Manufacturers currently maintain with Secondary Manufacturers. Even if Congress had delegated such broad authority, gap-filling rules that alter contracts and corporate legal assumptions would require more than mere guidance.²⁶

CMS’ proposal also conflicts with past practice. Historically, CMS has not required manufacturers to report Secondary Manufacturers’ data. CMS decided not to finalize such a proposal in a 2007 rule, after receiving comments that doing so would be “unduly burdensome on manufacturers, call into question the veracity of manufacturer pricing information reported to CMS, and potentially violate anti-trust statutes because [the CMS proposal] would require manufacturers to share pricing information and engage in anti-competitive practices.”²⁷

²² Guidance at Appendix C; ; Negotiation Data Elements under sections 11001 and 11002 of the Inflation Reduction Act ICR. Available at: <https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pa-listing/cms-10847>.

²³ SSA § 1193(a) (emphasis added).

²⁴ See also 1 U.S.C. 1, which provides that, “[i]n determining the meaning of any Act of Congress, unless the context indicates otherwise— words importing the singular include and apply to several persons, parties, or things; [and] words importing the plural include the singular. . . .”

²⁵ SSA § 1193(a)(5).

²⁶ *Perez v. Mortg. Bankers Ass’n*, 575 U.S. 92 (2015) (Guidance cannot have the force and effect of law).

²⁷ 72 Fed. Reg. 39199 (Jul. 17, 2007).

CMS concluded that requiring a primary manufacturer to include sales of a secondary manufacturer within its Average Manufacturer Price (AMP) calculation “would be problematic from an administrative accounting and anti-trust perspective.”²⁸

As was the case in 2007, it would be legally problematic, as well as infeasible, for innovator manufacturers to gather the vast amounts of data CMS is anticipating gathering – all prior to CMS’ October 1st, 2023 deadline for signing an Agreement under section 1193 with the Primary Manufacturer and October 2nd, 2023 deadline to submit extensive data and research to CMS. To report information to CMS, innovator manufacturers would likely have to access proprietary books and records of the Secondary Manufacturers, which may be competitors, raising a variety of business and legal issues. For example, section 50.1, explains that the Primary Manufacturer is required to submit “[c]urrent unit costs of production and distribution of the selected drug, averaged across the Primary Manufacturer and any Secondary Manufacturer(s).” Section 50.1 also anticipates that the Primary Manufacturer will collect “[m]arket data and revenue and sales volume data” from Secondary Manufacturers and blend the data with its own data. Section 50.1.1 states that the Primary Manufacturer “must submit data on [non-Federal average manufacturer price (non-FAMP)] for the selected drug for the Primary Manufacturer and any Secondary Manufacturer.” The Guidance, if adopted as final, raises the specter of anti-trust concerns to the extent it requires a Primary Manufacturer to collect and aggregate non-public, competitively sensitive Secondary Manufacturer information otherwise not accessible by the Primary Manufacturer.

Further, even if Primary Manufacturers could modify existing contractual agreements to ensure indemnification clauses, create firewalls to access proprietary information, and ensure information is available, there is simply insufficient time to do so prior to the deadlines for the 2026 IPAY (which require execution of CMS-manufacturer Agreements under section 1193 by October 1st, 2023, and certain information to be submitted by October 2nd, 2023). Indeed, it is not clear what unintended consequences CMS’ policy would have on the supply chain and/or collaboration among manufacturers to spur innovation, and CMS includes no discussion of how its requirements would affect current repackaging, relabeling, or authorized generic manufacturing activities.

For the reasons stated above, ***CMS must not adopt the Primary/Secondary Manufacturer policy.*** If more than one entity meets the definition of manufacturer, CMS may enter into separate Agreements with each manufacturer, as the statute already anticipates multiple Agreements with multiple manufacturers.

b. Entrance into Agreement with CMS and Compliance with Administrative Actions (Sections 40.1 and 40.5)

CMS states that it would use the Health Plan Management System to identify relevant points of contact, effectuate the Agreement, and store the Agreement, and that within “5 days following publication by CMS of the list of selected drugs for an initial price applicability year [September 1st, 2023, for the first year of the Program], if the Primary Manufacturer of a selected drug elects to enter into an Agreement with CMS...the Primary Manufacturer must submit to CMS all names, titles, and contact information for representatives authorized to execute the Agreement and conduct the negotiation.” CMS also notes that it “intends for the Agreement to contain the requirements discussed in sections 40.1 through 40.7 of this memorandum.” While CMS states it “will make reasonable efforts to make the final text of the Agreement available to the public before the selected drug list for initial price applicability year 2026 is published,” it has publicly indicated it will not likely seek comments on the Agreement itself. As the deadline for publication of the selected drug list is September 1st, 2023, CMS’ proposal for “final text” appears to mean that manufacturers will be required to sign, within a month (by October 1st, 2023), an Agreement they have never seen before and which they have only 30 days to review.

First, ***PhRMA recommends that CMS should not adopt its “5 days for review and decision” proposal.*** The statute (which gives as little as 30 days post-selection to decide whether to sign) is itself highly problematic, but

²⁸ Ibid at 39200.

does not authorize CMS to cut the 30-day decision period down to five days.²⁹ While PhRMA appreciates CMS attempting to identify authorized representatives early, requiring manufacturers to decide whether to “elect to sign” within five days would conflict with the statute’s later deadline of October 1st. Moreover, as long as an Agreement may be signed by the statutory deadline, CMS should view statutory obligations as fulfilled.

Second, ***PhRMA reminds CMS that it may not impose manufacturer requirements that go beyond the plain language of section 1193 of the SSA.*** Although in several places, CMS characterizes the Agreement as “voluntary” it is important to note that the IRA price-setting provisions are distinct from an ordinary contract or grant relationship, where an entity submits a bid or proposal in response to a solicitation. The 1193 Agreement cannot be described as voluntary. Instead, the Agreement is properly understood as a contract of adhesion, signed under duress. Manufacturers of selected drugs have little recourse other than to sign the Agreements. If the manufacturer does not enter into the Agreement by the required date (October 1st, 2023, for the first year of the Program), the manufacturer is subject to per-day excise taxes starting at almost twice the sales of the selected drug and increasing to 1,900 percent of a drug’s total revenues.³⁰ While this up-to 1,900 percent assessment is framed as a “tax,” Congress understood that it would function as a penalty forcing manufacturers to subject themselves to the government’s so-called “agreement.” For example, the Joint Committee on Taxation estimated that the “tax” would raise zero revenue, because no manufacturer could possibly afford to pay such an astronomical assessment.³¹ Further, to suspend imposition of the possibility of crippling excise taxes under the IRA, a manufacturer must terminate “all” applicable agreements under Medicaid and Medicare Part D,³² resulting in the termination of coverage in Medicaid and Medicare Parts B and D for all of the manufacturer’s products – not just the selected product – when almost half of annual nationwide spending on prescription medicines is through Medicare and Medicaid.³³

Because the IRA sidesteps a true negotiation in any sense of the term, CMS cannot use the Agreement to bind manufacturers to requirements that go beyond the plain language of section 1193 and claim manufacturers “agreed” to the terms. CMS has also previously noted that statutory agreements that function similar to the 1193 agreement are not “contracts” or true “agreements” but merely a notification of the statutory provisions governing the Program. With respect to the Medicaid National Drug Rebate Agreement (NDRA), CMS noted:

The NDRA is not a contract. Rather, it should be viewed as an opt-in Agreement that memorializes the statute and regulations. Therefore, we noted our intention to use the updated NDRA as a standard agreement that will not be subject to further revisions based on negotiations with individual manufacturers.³⁴

Third, ***PhRMA recommends CMS share the Agreement text itself for a meaningful period of comment.*** Without seeing the Agreement text and being afforded a period of comment, it is unreasonable for CMS to conclude that innovator manufacturers will simply review and sign, all in a one-month period. In past situations,

²⁹ SSA §§ 1191(b)(4)(A); 1191(d)(2). In other cases, those entering into agreements have more time to review. The Coverage Gap Discount Program agreement allowed a 30-day review period. The VA offers a rolling submission process. The Medicaid rebate program has another approach that implements the agreement 60 days after the end of the quarter. *See e.g.*, 42 CFR § 423.2315(c); <https://www.medicaid.gov/medicaid/prescription-drugs/medicaid-drug-rebate-program/medicaid-national-drug-rebate-agreement-ndra/index.html>; <https://www.va.gov/opal/nac/fss/pharmaceuticals.asp>; <https://www.va.gov/opal/docs/nac/fss/vaSolicitationM5Q50A03R8.zip>.

³⁰ 26 U.S.C. 5000D(b)(1)(A). *See also* Congressional Research Service, *Tax Provisions in the Inflation Reduction Act of 2022*, tbl. 2 (2022) (confirming a top excise tax of 1,900 percent).

³¹ Joint Commission on Taxation, *Estimated Budget Effects of the Revenue Provisions of Title XIII - Committee On Ways And Means, of H.R. 5376, The “Build Back Better Act,” As Passed by the House of Representatives, Fiscal Years 2022–2031*, at 8 (Nov. 19, 2021), <https://bit.ly/3plC4cd> (“no revenue effect”); *accord* Letter from P.L. Swagel, Director, CBO, to Hon. F. Pallone Jr., Chairman, Committee on Energy and Commerce (Oct. 11, 2019), at 14. Available at: <https://bit.ly/3osZPzX> (noting JCT had concluded, of identical predecessor provision, that “manufacturers would either participate in the negotiation process or pull a particular drug out of the U.S. market entirely”).

³² 26 U.S.C. 5000D(c).

³³ CBO, *Prescription Drugs: Spending, Use, and Prices* at 8 (2022).

³⁴ 83 Fed. Reg. 12770, 12771 (March 23, 2018).

CMS has provided the text of the draft agreement and requested comments before finalizing the agreement.³⁵ Without knowing exactly how the Agreement will read for this Program, it is not possible to anticipate every potential comment on the contours of the Agreement.

Fourth, and finally, ***PhRMA recommends CMS not include in the Agreement open-ended language that seeks to bind manufacturers to unknown requirements or ambiguous terms.*** CMS states in section 40.5 that “after entering in an Agreement with CMS...the Primary Manufacturer must comply with requirements determined by CMS to be necessary for purposes of administering the Negotiation Program and monitoring compliance with the Negotiation Program.” CMS does not offer additional information as to what exactly it intends to include as a result of this statement. However, even if the Agreement were a true contract – which, as discussed above, it is not – parties to a contract cannot be “bound to unknown terms which are beyond the range of reasonable expectation.”³⁶

c. Submission of Data to Inform Negotiation (Section 40.2)

Under the timetable described in the Guidance, manufacturers of selected drugs will only have 30 days after the list of selected drugs is published to prepare and submit information to CMS. Thirty days is a woefully inadequate period of time for manufacturers to gather and submit the data that will be used in price setting. CMS has authority to allow flexibility on submission of data beyond October 2nd, 2023, and should use that authority to provide additional time for manufacturers to submit robust data and research to support MFP determinations. CMS or manufacturers may also find that there must be an opportunity to submit additional information to resolve issues, answer specific questions, or address misunderstandings in how CMS is interpreting data or data submission requirements. The deadline of October 2nd, 2023 arguably applies only to the data specifically mentioned in section 1193(a)(4) (that is, non-FAMP data). This analysis would harmonize the following statutory provisions:

- Section 1194(b)(2)(A), which, as amended by 1191(d)(5), states “Not later than October 2, 2023, the manufacturer of the drug shall submit to the Secretary, in accordance with section 1193(a)(4), the information *described in such section*” (emphasis added);
- Section 1193(a)(4), which “describes” non-FAMP information as well as “information that the Secretary requires to carry out the negotiation (or renegotiation process) under this part”; and
- Section 1194(e), which requires certain information for price setting, but is not cross-referenced in section 1193(a)(4).

The IRA also states that the Secretary may specify the “manner” in which data are submitted. The fact that the statute fails to “describe” an October 2nd, 2023 deadline for submitting data to support consideration of the section 1194(e) factors, along with the discretion the Secretary maintains to dictate the manner of submission, allows CMS some flexibility on timelines. This flexibility provides the Agency an important opportunity to facilitate a more effective implementation of the Program by permitting submission of additional or updated data and research after October 2nd. ***PhRMA recommends that CMS read the statute in a manner that ensures adequate time to gather information and submit data on the 1194(e) factors, and not to adhere to an arbitrary and rigid deadline of October 2nd if there are other, more reasonable ways to interpret the language.*** Further, we urge the Agency to specify opportunities for manufacturers to submit additional data after October 2nd, including manufacturer-specific data under section 1194(e)(2).

d. Confidentiality of Proprietary Information (Section 40.2.1)

³⁵ 81 Fed. Reg. 78816 (Nov. 9, 2016).

³⁶ Restatement (Second) of Contracts § 211 (1981).

PhRMA appreciates CMS' recognition that a large amount of the data to be submitted by manufacturers, including non-FAMP data³⁷, is highly sensitive and proprietary. In Appendix C, CMS includes ten pages of definitions relating to "manufacturer-specific" information to be submitted by October 2nd, 2023. Separately, CMS recently released a 45-page form for collecting information.³⁸ Despite these robust submission requirements, the Guidance fails to describe, and therefore does not provide opportunity for comment on, the details of the robust confidentiality policy that must accompany companies' submission of manufacturer-specific data. We discuss this concern in more detail below and provide suggested minimum requirements for a confidentiality policy.

PhRMA is unaware of any other program that would compile such a large volume of biopharmaceutical innovator information in one repository – on R&D, patent, cost, pricing, and other highly sensitive data. Congress seemingly was aware of the sensitivity of data to be submitted, as it included in the IRA an unusually restrictive limitation, applying not just to disclosure of manufacturer-submitted data but also their "use." Only the Secretary (or Comptroller General in certain situations) may use the data, and then, only to carry out the price-setting Program.³⁹

While CMS acknowledges it will adopt a confidentiality policy, it does not propose such a policy for comment, and states only that such policy would be "consistent with existing requirements for protecting proprietary information, such as Exemption 4 of the Freedom of Information Act (FOIA)." However, Exemption 4 of FOIA addresses disclosure, not use, and nothing in the IRA directs CMS to use FOIA as the basis for its confidentiality and security protocols. Further, Exemption 4 would not by itself adequately protect the proprietary information the IRA requires. While PhRMA urges CMS to adopt the procedures of FOIA regulations allowing innovators to designate part or all of the information submitted as proprietary,⁴⁰ CMS must also develop a robust confidentiality policy, shared with manufacturers for feedback.

CMS' cursory, one-line explanation of a "confidentiality policy" provides little assurance to manufacturers that their highly valued information will be protected. At a minimum, any confidentiality policy must require:

- Access to any information received is limited to the smallest number of employees and other personnel possible, as well as the minimum data necessary, and such personnel are inventoried and recorded on a regular basis (including an explanation of such individual's legitimate need to use the information and purpose);
- Execution of non-disclosure agreements by any individuals with access to the data (including contractors and staff) as a pre-condition to access, under which they are restricted from improperly using or disclosing any proprietary information received, during their employment/engagement and in perpetuity post-employment;
- Destruction of data by any individuals with access to the data when any Agreement terminates. CMS, the Comptroller General, or any part of the U.S. Department of Health and Human Services (HHS) that accesses information maintains policies as to how and when it will destroy proprietary information of the manufacturer, informs the manufacturer of such destruction, and documents compliance with destruction policies;

³⁷ Non-FAMP is the average price paid by wholesalers for drugs distributed to non-federal purchasers. Manufacturers calculate this on a quarterly basis and report it to the U.S. Department of Veterans Affairs (VA); this calculated price includes any rebates, cash discounts or other price reductions but excludes any discounts given to federal purchasers. Manufacturer rebates, discounts, and other price reductions are confidential and proprietary and non-FAMP, as used today with the VA, is not a publicly available metric.

³⁸ 88 Fed. Reg. 16983 (March 21, 2023); <https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pralisting/cms-10847>.

³⁹ SSA § 1193(c).

⁴⁰ 45 C.F.R. § 5.41.

- Notification to any submitters of any erroneous use or disclosure of proprietary information, even if inadvertent, and how it intends to remedy such use or disclosure;
- Notification to manufacturers any time data are shared outside of CMS (for example with a contractor) or CMS intends to use such data for purposes unrelated to price setting (for example, because CMS determines the data are not proprietary), the rationale for such sharing/use, and providing manufacturers with a robust prior opportunity to object to such sharing/use, along with an adjudication process. If CMS determines that otherwise proprietary information is nevertheless “publicly available,” CMS should explain such reasoning prior to allowing such information to be used (and provide for a period of adjudication before the data could be shared or released). Again, such notification must extend not just to public disclosure, but also any “use” or disclosure outside CMS, including to Congress or other agencies; and
- Referrals made to the Department of Justice regarding violations of criminal laws prohibiting the publication, divulging, disclosure, or making known in any manner or to any extent not authorized by law, trade secret or confidential commercial information.⁴¹

The government has a history of requiring non-disclosure agreements from contractors and others under agreement, and PhRMA is happy to share templates. Exhibit B, attached to this comment letter, is one such template. Clauses CMS should add to any contracts or other Agreements include HHS Acquisition Regulations (HHSAR) 352.224-71, and clauses similar to H.6, or the “Disclosure of Information” provision, respectively, at the sites below:

- <https://www.hhs.gov/sites/default/files/gram-contract.pdf>; and
- <https://www.hhs.gov/sites/default/files/vaccine-agreement-with-glaxo-smith-kline-modifications-1-and-2.pdf>.

CMS should put forward a security policy as well, explaining how it will ensure the cybersecurity of systems holding manufacturer-specific data. The security protocol must include limited access to only certain personnel via secure portal; procedures on secure encrypted transmission mechanisms (as approved by HHS’ Chief Information Officer and Office of the General Counsel); secure storage; inability to download confidential information to removable media or any other portable storage; policies on and tracking of any printing or screenshotting of confidential information (including watermarking of electronic and paper copies with a “confidential” label, safeguards that only a minimum amount may be printed, and standards that printouts remain within a particular physical location from which they cannot be removed, along with locked offices and file cabinets).

CMS should periodically audit and report on its use of confidential commercial information, as well as compliance with its confidentiality and security protocols.

For the reasons stated above, ***PhRMA recommends that CMS protect confidential information beyond the protections of FOIA Exemption 4, share its confidentiality policy for comment, and ensure contractors and others with access to manufacturer data have agreements with CMS that adequately protect the high volumes of proprietary information CMS will collect.***

PhRMA also asks that CMS clarify that the existence of and status of a pending NDA or BLA, in addition to information contained in a pending NDA or BLA, will be treated as proprietary information under SSA section

⁴¹ 18 U.S.C. 1905.

1193(c) and as trade secret and/or confidential commercial information that is protected from disclosure under Exemption 4 of the FOIA, 5 U.S.C. § 552(b)(4).

This clarification is needed because section 40.2.1 of the Guidance states that “CMS intends to treat the data on prior Federal funding and approved patent applications, exclusivities, and *applications and approvals* under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Services Act as non-proprietary because CMS believes these data are available publicly.” The use of the term “applications and approvals” suggests that both pending and approved applications might be treated as non-proprietary. The “applications and approvals” language also appears in Appendix C (Definitions), which states that “[a]ctive *and pending* FDA applications and approvals includes...all applications for approval under section 505(c) of the Federal Food, Drug, and Cosmetic Act or sections (sic) 351(a) of the Public Health Service Act, *including those not yet decided...*” (emphasis added).

PhRMA disagrees that “these data are available publicly.” On the contrary, information in pending marketing applications is typically proprietary and highly sensitive and is protected from disclosure by federal law. This sensitivity remains after approval, with much data and information in approved applications remaining protected confidential commercial information and trade secrets exempt from disclosure. Under FDA’s regulations, the existence and status of a pending application, in addition to information contained in a pending NDA or BLA, generally are protected from public disclosure.⁴² FDA adopted this regulation to implement the Federal Trade Secrets Act, FOIA, and section 301(j) of the FD&C Act, which all protect such information from public disclosure, and has long regarded this information as competitively sensitive for which disclosure would cause competitive harm.⁴³ Only once a decision on an application is final will certain information regarding the application be subject to potential disclosure, and even then, other information within the application remains protected.⁴⁴ Consistent with the fact that FDA protects information about and in pending marketing applications from disclosure, CMS’ Guidance should be revised to provide that CMS will treat such information as proprietary under SSA section 1193(c) and as trade secret and/or confidential commercial information under FOIA. Indeed, the fact that CMS has misidentified these data as publicly available further underscores the need to rely upon a manufacturer’s indication that data are proprietary and not in the public domain.

Finally, CMS notes that it will publish an explanation for the MFP by March 1st, 2025, and may make “high-level comments about the data submitted to CMS, without sharing any proprietary information,” such as saying that the “manufacturer has recouped its R&D costs.” In making any such high-level statement, the Agency should be specific about its limitations.⁴⁵ CMS is defining R&D in ways that differ from the ways that the biopharmaceutical industry does. The industry definition as a matter of course includes costs for all failures and

⁴² See 21 C.F.R. §§ 314.430(b) (“FDA will not publicly disclose the existence of an application...before an approval letter...or tentative approval letter is sent to the applicant..., unless the existence of the application...has been previously publicly disclosed or acknowledged.”); id. § 314.430(c) (“If the existence of an unapproved application or abbreviated application [for a small molecule drug] has not been publicly disclosed or acknowledged, no data or information in the application or abbreviated application is available for public disclosure.”); id. § 601.51(b) (“The existence of a biological product file will not be disclosed by [FDA] before a biologics license application has been approved unless it has previously been publicly disclosed or acknowledged.”), id. § 601.51(c) (“If the existence of a biological product file has not been publicly disclosed or acknowledged, no data or information in the biological product file is available for public disclosure.”); see also 39 Fed. Reg. 44,602, 44,634 (Dec. 24, 1974) (“The existence of a pending NDA constitutes confidential commercial information where the existence of clinical testing has not previously been publicly disclosed or acknowledged.”)

⁴³ 39 Fed. Reg. at 44,634

⁴⁴ 21 C.F.R §§ 314.430(f), (g), 601.51(e), (f)

⁴⁵ CMS should also remain mindful of international commitments to protect undisclosed information from being disclosed or unfairly used, particularly under Article 39 of the WTO TRIPS Agreement. Failure to protect confidential information, including in any “high-level” statements, would be contrary to international commitments of the United States.

successes and doesn't distinguish between them.⁴⁶ Thus, "high-level" statements should not provide misleading information that extends beyond CMS' unique definitions and its price-setting scheme.

e. Data Use Provisions and Limitations (Section 40.2.2)

PhRMA strongly opposes provisions of the Guidance that would prohibit manufacturers from disclosing information exchanged verbally or in writing that relates to basic elements of CMS' MFP decision-making process. These provisions lack legal authority, hinder government accountability, and prevent ongoing, year-to-year learning that will be important to the effective implementation of and manufacturer compliance with the Program. We urge CMS to delete these provisions and adopt an approach that promotes transparency and accountability in government decision-making while protecting proprietary and confidential information.

Specifically, in section 40.2.2 of the Guidance, CMS cites to general authority for "administering the program and monitoring compliance," to propose a sweeping policy that would restrain manufacturer speech by placing limits on what a manufacturer can use or disclose from CMS' offers, including the ceiling price, the information contained in any concise justification provided with an offer, and any information exchanged verbally during the "negotiation" period. CMS would prohibit audio or video recording of any oral conversations between CMS and a manufacturer, and even limit use – stating that manufacturers could use government information only for purposes of the Program, and as required by applicable state or federal law.

The Agency also proposes a "Certificate of Data Destruction," to be submitted within 30 days of a drug or biologic no longer qualifying as a selected drug. Under such certificate, a manufacturer would certify that all information received from CMS during the "negotiation" period and potential "renegotiation" period(s), including the initial offer and any subsequent offers, and the concise justification(s), and any of the manufacturer's written notes or emails pertaining to negotiation (or renegotiations) with CMS, have been destroyed.

PhRMA is unaware of CMS or HHS ever having proposed such an over-broad and patently unconstitutional information policy. Prior governmental restraints on speech "are the most serious and the least tolerable infringement on First Amendment rights,"⁴⁷ and they are subject to a "heavy presumption against [their] constitutional validity."⁴⁸ Indeed, restraints on the disclosure of "truthful information about a matter of public significance" – like the data subject to use restrictions in section 40.2.2 – are almost never permissible under the First Amendment.⁴⁹ The Supreme Court has recognized a limited exception to that rule for information that cannot be disclosed without doing substantial, concrete, and immediate harm, such as when necessary to protect "the secrecy of information important to our national security."⁵⁰ However, the information at issue here is plainly not of that type.⁵¹

⁴⁶ PhRMA's definition of R&D expenditures reported in its Annual R&D Survey (<https://phrma.org/resource-center/Topics/Research-and-Development/2022-PhRMA-Annual-Membership-Survey>) includes basic and applied research, as well as developmental activities carried on or supported in the pharmaceutical, biological, chemical, medical, and related sciences, including psychology and psychiatry, if the purpose of such activities is concerned ultimately with the utilization of scientific principles in understanding diseases or in improving health. When reporting industry R&D expenditures, members include the total cost incurred for all pharmaceutical R&D activities including salaries, materials, supplies used, a fair share of overhead (administration, depreciation, space charges, rent, etc.), as well as the cost of developing quality control. Also included are expenditures within the company's U.S. (inside)/foreign (outside) research laboratories plus R&D funds contracted or granted to commercial laboratories, private practitioners, consultants, educational and nonprofit research institutions, manufacturing and other companies, or other research-performing organizations located inside/outside of the United States. These **do not** include the cost of routine quality control activities, capital expenditures, or any costs incurred for drug or medical R&D conducted under a grant or contract for other companies.

⁴⁷ *Nebraska Press Ass'n v. Stuart*, 427 U.S. 539, 559 (1976).

⁴⁸ *Org. for a Better Austin v. Keefe*, 402 U.S. 415, 419 (1971) (quotation marks omitted).

⁴⁹ *Bartnicki v. Vopper*, 532 U.S. 514, 527 (2001) (citation omitted).

⁵⁰ *Snepp v. United States*, 444 U.S. 507, 509 n.3 (1980).

⁵¹ See *McGehee v. Casey*, 718 F.2d 1137, 1141 (D.C. Cir. 1983) ("The government has no legitimate interest in censoring unclassified materials.").

Indeed, section 40.2.2 does not claim that its data use restrictions would satisfy strict scrutiny – i.e., that they serve a compelling state interest and are narrowly tailored to achieve that interest. Much less does CMS offer actual “empirical evidence” to substantiate the need for such restrictions,⁵² nor can CMS defend the data use restrictions in section 40.2.2 on the ground that manufacturers enter the price setting process voluntarily. In fact, as noted above, participation by manufacturers is not truly voluntary, as the manufacturer’s ability to opt out of the program is highly limited, both as a practical and legal matter. But even if participation were voluntary, “[t]he government may not censor [truthful, non-classified information], ‘contractually or otherwise.’”⁵³ Simply put, the government may not impose a “direct regulation of speech...as a condition on the receipt of federal funds” where, as here, the condition goes “beyond ensuring that federal funds [are] not...used to subsidize” unwanted speech.⁵⁴

Section 40.2.2’s document-destruction requirements similarly constitute impermissible restrictions on the freedom of speech. Indeed, the requirement to destroy information “receive[d] during the negotiation period from CMS” goes a significant step further even than a prior restraint on publication. It is hard to imagine almost any scenario (outside the national security context) in which the government can justify forcing a private individual to destroy the individual’s own property – even the individual’s own notes – in order to prevent truthful information from getting out. Taken literally, the Guidance would require manufacturers to destroy emails, notes, and other records of their own internal company deliberations, so long as those deliberations “pertain[] to negotiations,” regardless of whether the records reflect information from CMS itself. As noted below, the policy would also prevent manufacturers from reporting inappropriate or unlawful behavior by CMS or its employees and officials, since such disclosures are usually not “required by applicable state or federal law.” The government has no legitimate interest – much less a compelling interest – in commanding such a result.

Section 40.2.2 violates the First Amendment in other ways as well. The prohibition on using price setting data “for any purpose other than the Medicare Drug Negotiation Program” is impermissibly vague. Vague laws inherently invite subjective enforcement, a concern that is heightened when speech is at issue.⁵⁵ For that reason, “a more stringent vagueness test” applies where, as here, the government attempts to restrict private speech.⁵⁶ If taken at face value, CMS’ prohibition would apply to a manufacturer’s internal deliberations, akin to an individual’s internal thought process; such a prohibition would be substantially overbroad and would fail strict scrutiny. But even if CMS would read the prohibition more narrowly – something it is not possible to discern from the Guidance itself – the Guidance’s failure to specify its scope with reasonable precision threatens to chill legitimate speech and invites arbitrary enforcement.⁵⁷

For information that is not proprietary to the manufacturer, the proposal also is at odds with government records retention and freedom of information principles. For example, for non-proprietary information held in government custody, the government ordinarily is required to disclose such data if requested under FOIA.⁵⁸ Thus, while information *held by the government* might be subject to records requests under FOIA, CMS would simultaneously require a *manufacturer* to hide or destroy the same information. Presumably, when the information is in government custody, it would be subject to Federal Records Act⁵⁹ requirements, under which the Agency would be required to maintain the records, document its activities, file records for safe storage and efficient retrieval, and dispose of records only according to an Agency schedule.

⁵² *United States v. Playboy Enter. Grp., Inc.*, 529 U.S. 803, 816 (2000).

⁵³ *McGehee*, 718 F.2d at 1141 (quoting *United States v. Marchetti*, 466 F.2d 1309, 1313 (4th Cir. 1972)).

⁵⁴ *Agency for Intern’l Dev. v. Alliance for Open Society Intern’l, Inc.*, 570 U.S. 205, 213-15 (2013).

⁵⁵ *See Grayned v. City of Rockford*, 408 U.S. 104, 109 (1972) (“[W]here a vague [law] abuts upon sensitive areas of basic First Amendment freedoms, it operates to inhibit the exercise of those freedoms.”) (cleaned up).

⁵⁶ *Village of Hoffman Estates v. Flipside, Hoffman Estates, Inc.*, 455 U.S. 489, 499 (1982).

⁵⁷ *See Grayned*, 408 U.S. at 108-09.

⁵⁸ 5 U.S.C. 552.

⁵⁹ 44 U.S.C. 31.

Far from allowing CMS to “administer the program” and “monitor compliance,” the provisions would have the effect of undermining sound program administration and consistent compliance by foreclosing vital opportunities for program transparency. Manufacturers that undergo the MFP decision-making process would effectively be muzzled from pointing out flaws, oversights, or methodological problems in CMS’ administration of the Program or its compliance monitoring. Further, CMS’ proposal would impede the year-to-year learning by stakeholders that would serve an important role in effective program administration and compliance.

It is unclear if the policy would apply to sharing or retaining information with respect to attorneys, accountants, or others performing due diligence on a company’s activities or providing the company with legal advice. Even within the same corporation, a manufacturer would not have the data to inform activities on a second set of selected drugs. The degree of secrecy imposed by these provisions creates the impression of an Agency unwilling to subject its decisions to open, evidence-based scrutiny, creating a significant risk of undermining public trust in CMS decision-making. With the public explanation of the MFP occurring many months after the end of the price setting period (on March 1st, 2025) and a full 17 months after the sole, limited opportunity for the public to provide input, the public and those relying on medicines or certain forms of medicines that could be affected by CMS price setting may question why CMS felt the need to shield its decision-making process from scrutiny in this way. ***For the reasons stated above, CMS should abandon the proposed data use restrictions on disclosing and/or using government-provided data as the policy violates the First Amendment, conflicts with government transparency principles, and cannot be finalized.***

In a recent blog-post CMS stated: “CMS continues to believe that transparency promotes accountability.”⁶⁰ We agree, and believe such transparency must start with the Agency itself.

f. Effectuation of the MFP (Section 40.4)

Under section 1193(a) of the SSA, manufacturers entering into an Agreement with CMS must provide access to the MFP for selected drugs that are covered under Part D to (1) MFP-eligible individuals and (2) pharmacies, mail order services, and other dispensers with respect to such MFP-eligible individuals who are dispensed such drugs. CMS notes in the guidance that the IRA requirement that the negotiated price for a selected drug be less than or equal to the MFP plus a dispensing fee for MFP-eligible individuals⁶¹ “ensures that Part D MFP-eligible individuals will have access to the MFP at the point-of-sale.”⁶² In addition, CMS would define “providing access to the MFP” in the context of dispensing entities as ensuring the amount paid by the dispensing entity is not greater than the MFP. Furthermore, CMS intends to require Primary Manufacturers to provide access to the MFP in one of two ways: (1) by ensuring that the price paid by the dispensing entity is no greater than the MFP; or (2) by providing retrospective reimbursement for the difference between the dispensing entity’s actual acquisition cost and the MFP.⁶³

It is critical that the Agreement reflect such options and ensure that manufacturers are only required to provide access to the MFP after receiving data to verify eligibility.

While we appreciate CMS’ clarity on options for providing access to the MFP, PhRMA has significant concerns that the resulting process will add burden to all stakeholders in the pharmaceutical supply chain, significantly increase risks to program integrity, and ultimately impact the Agency’s ability to implement the IRA in a successful and orderly manner unless CMS: (1) ensures manufacturers receive data needed to verify MFP eligibility and 340B drug status; (2) removes the requirement for manufacturers to reimburse intermediate entities

⁶⁰ CMS. (2023). CMS Drug Spending Dashboards and the Inflation Reduction Act. Available at: <https://www.cms.gov/blog/cms-drug-spending-dashboards-and-inflation-reduction-act>.

⁶¹ SSA § 1860D-2(d)(1)(D) (as amended by IRA 11001(b)) (Part D negotiated price for a selected drug must be less than or equal to the MFP plus a dispensing fee).

⁶² Guidance, p. 31.

⁶³ Guidance, p. 32.

within 14 days; and (3) uses a more widely available pricing benchmark to define the MFP discount amount. PhRMA strongly urges the Agency to work towards a solution (clarified in guidance), that would:

- ***Provide manufacturers with access to certain data fields from the Part D Prescription Drug Event (PDE) records that will enable manufacturers to verify that a patient is an MFP-eligible individual.*** The statute does not require a manufacturer to provide access to the MFP for an individual who is not an “MFP-eligible individual”⁶⁴ and therefore, data need to be available to a manufacturer to verify an individual’s eligibility for the MFP prior to payment. Similarly, a manufacturer will need appropriate data to provide 340B covered entities (CEs) with the lesser of the MFP and 340B ceiling price, as well as to prevent payment of both an MFP statutory discount and a 340B discount on the same unit as is expressly prohibited under the MFP/340B nonduplication clause.⁶⁵ Without access to data for verification, we believe there could be significant disruptions to the Agency’s implementation of the IRA, and a significant risk of non-MFP eligible individuals receiving access to the MFP in contradiction to the statute. CMS should expressly acknowledge that manufacturers will establish, receive, review, and as necessary, audit MFP validation data to ensure manufacturers have provided MFP access in accordance with the statute. A list of the minimum needed data fields is included as Exhibit A to this comment letter.
- ***Remove the requirement for manufacturers to reimburse applicable intermediate entities within 14 days for manufacturers choosing a retrospective approach to providing access to the MFP.*** To meet the required payment deadline to pharmacies and other dispensers (hereafter referred to jointly as pharmacies), manufacturers could contract with intermediate entities to facilitate payments to pharmacies in a timely manner, provided those intermediate entities are given access to claims-level transaction data. However, manufacturers need more time than the 14 days proposed by CMS to review claims and verify patient eligibility for the MFP. PhRMA strongly recommends that CMS eliminate the requirement to reimburse intermediate entities within 14 days and instead provide flexibility for intermediate entities and manufacturers to develop processes and set contractual terms related to timing of payment.
- ***Utilize a widely available pricing benchmark such as Wholesale Acquisition Cost (WAC) to define the amount of MFP discounts.*** Acquisition cost is an inappropriate metric to use for defining the amount of MFP discounts. It is currently known solely at the prescription level by the dispensing pharmacy and requiring pharmacies to report the acquisition cost to other stakeholders in the supply chain – who could be playing key coordinating roles in facilitating payment of MFP discounts – could harm competitive incentives in the pharmaceutical supply chain.

PhRMA urges the Agency to improve effectuation of the MFP and minimize stakeholder burden by designating a third-party administrator (TPA) to facilitate this process for manufacturers choosing a retrospective approach. This will best ensure consistent patient access to the MFP at the point-of-sale, enable full reimbursement to pharmacies through a standardized process within the 14-day time frame proposed by CMS, protect program integrity, promote efficiency and accuracy, and minimize stakeholder burden.

If CMS believes it is unable to modify the Guidance to address the three issues noted above, PhRMA strongly urges CMS to withdraw section 40.4 from the revised Guidance. The Agency should instead continue to work with stakeholders to address these issues to meet the needs of all entities within the pharmaceutical supply chain.

PhRMA’s additional feedback on this section of the Guidance follows below.

⁶⁴ SSA § 1191(c)(2) and section 80 of the Guidance.

⁶⁵ SSA § 1193(d)

CMS Needs to Provide Manufacturers with Access to Claims Data for Verification

With or without designating a TPA, CMS must, at a minimum, articulate a process by which manufacturers will receive access to detailed claims data necessary to verify claims, regardless of whether the manufacturer chooses to make the MFP discount available upfront or on a retrospective basis. Manufacturer access to these data is imperative for protecting program integrity. A list of minimum data fields is included as Exhibit A to this letter, and we recommend that CMS seek stakeholder feedback before finalizing this list of data fields.

PhRMA believes it is important for CMS to make these data available to manufacturers, and to do so in an easily accessible format. Manufacturers cannot rely on entering into private contracts with other supply chain stakeholders to secure the data necessary for verification, as these stakeholders may not have access to all required claims-level data elements. For example, if a manufacturer were to contract with a wholesaler to provide pharmacies with access to the MFP, the wholesaler may not have access to the claims-level detail needed for manufacturer verification without significant changes to the existing chargeback system or intervention from CMS.

The Agency's Example of Effectuating the MFP in Section 90.2 of the Guidance is Missing Critical Information Flows Needed to Verify Claims

In section 90.2 of the Guidance (“Monitoring Access to the MFP”), CMS provides an example of how private sector stakeholders could leverage existing systems for manufacturers to provide access to the MFP. Specifically, CMS details a chargeback from a wholesaler to a manufacturer for a retrospective MFP discount to a pharmacy.

Several elements of this example – in which wholesalers would invoice manufacturers for retrospective MFP discount chargebacks – are incompatible with the existing pharmaceutical supply chain infrastructure. First, the MFP must be made available on individual claims, but wholesalers do not currently engage in claims-level data transactions with pharmacies. Either pharmacies would need to begin reporting claims-level data to wholesalers, a burdensome reporting requirement that pharmacies may have significant reservations about undertaking, or wholesalers would need to be given access to portions of PDE data to obtain claims-level data necessary to correctly bill manufacturers for chargebacks.

Second, the Agency’s description in section 90.2 describes two “existing mechanisms” to ensure dispensing entities have access to the MFP and to verify that the MFP is only received by MFP-eligible individuals. However, the two mechanisms described by CMS – the RxBIN and Part D processor control number (RxPCN) – are not sufficient pieces of information for a manufacturer to fully verify eligibility for the MFP. For example, it would not be possible from just the RxPCN and RxBIN to identify which medicine is being dispensed, or to confirm that a transaction was not a duplicate or was not later reversed or revised. As noted above, Exhibit A to this comment letter includes a list of minimum fields that are needed for manufacturers to accurately verify eligibility of claims for MFP discounts, and to accurately identify claims subject to 340B discounts.⁶⁶ Most of these fields already appear on the Part D PDE record (and many are already provided to manufacturers under the Coverage Gap Discount Program), thus minimizing the reporting burden. PhRMA recommends that the Agency periodically reevaluate data elements necessary to verify MFP eligibility, with industry input, to help minimize operational shortcomings.

The Agency's Proposed Requirement for Manufacturers to Ensure Full Reimbursement to Dispensers and Intermediate Entities, as Applicable, is Not Possible as Drafted within 14 Days

⁶⁶ Accurate identification of claims subject to 340B agreements is necessary to ensure manufacturers provide 340B CEs access to the lesser of the MFP or 340B ceiling price.

PhRMA has significant concerns with the Agency's proposed requirement for manufacturers to reimburse any intermediate entities involved in effectuating the MFP within 14 days.

Under the Coverage Gap Discount Program (CGDP), Part D plans (or pharmacy benefit managers (PBMs) acting on their behalf) pay coverage gap discounts on behalf of manufacturers at the time of pharmacy adjudication (which, under prompt pay requirements, occurs within 14 days). But a key reason this system is possible is that manufacturer verification of coverage gap discount claims is permitted on a quarterly basis, some time after the 14-day timeframe for payment to the pharmacy.

PhRMA appreciates the need for timely reimbursement to pharmacies, but we strongly urge CMS to strike the language that would require reimbursement to intermediate entities within the same 14-day window as the pharmacy.⁶⁷ This would enable manufacturers to contract with intermediate entities for more time to perform claims verification after pharmacies have been fully reimbursed, as PhRMA does not believe that proper claims verification is possible within the 14-day window. Under the CGDP, for example, manufacturers have 38 days from receipt of an invoice from the CGDP TPA, Palmetto, to pay coverage gap discount obligations. The same 38-day payment window from receipt of invoice also applies to manufacturer rebate obligations under the Medicaid Drug Rebate Program. Indeed, under the Part D program today, plans submit PDE entries to CMS on a two-week cycle. So, CMS itself would barely receive data necessary for verification within the 14-day reimbursement window, let alone have time to make those data accessible to manufacturers for verification.

Acquisition Cost is an Inappropriate Metric to Define the Amount of an MFP Discount

In section 40.4 of the Guidance, CMS proposes that Primary Manufacturers choosing to provide access to the MFP through retrospective reimbursement will need to provide the pharmacy with a discount equal to the difference between the pharmacy's acquisition cost and the MFP.

PhRMA has significant concerns with the Agency's proposal. Acquisition cost is an inappropriate metric for several reasons, including: (1) the dispensing pharmacy's true acquisition cost for an individual prescription is currently unknown to entities outside of the pharmacy; and (2) reporting of the acquisition cost could harm competitive incentives in the pharmaceutical supply chain. Instead, PhRMA urges CMS to exercise its authority under section 1196 of the SSA and define a retrospective MFP discount based on a widely available pricing benchmark like WAC. Specifically, section 1191(a)(4) directs the Secretary to "carry out the...administrative duties...in accordance with section...1196," which, in turn, provides for "[t]he establishment of procedures to carry out the provisions of [the Medicare Drug Price Negotiation Program], as applicable, with respect to [MFP-eligible individuals]."

Pharmacies may purchase medicines from multiple wholesalers at different prices, and the quantity purchased can vary significantly. Individual prescriptions are often comprised of a quantity of medicine pulled from larger bottles received from wholesalers and can even be comprised of a quantity taken from bottles purchased from different wholesalers at different prices depending on the available inventory at the pharmacy. Because of this, only the dispensing pharmacy would be in a position to know the true acquisition cost for a prescription dispensed to an MFP-eligible beneficiary. Wholesalers or other supply chain stakeholders do not currently have insight into the acquisition cost at the prescription level, nor do manufacturers since they typically do not sell medicines directly to pharmacies.

Furthermore, requiring pharmacies to report the acquisition cost for each prescription to intermediate entities for purposes of MFP effectuation has the potential to harm competitive incentives in the pharmaceutical supply chain. For example, if pharmacies are required to include acquisition cost data as part of the claim transaction, this could create incentives for Part D plans and PBMs to limit reimbursement to no more than the reported acquisition cost

⁶⁷ The IRA is silent on providing access to the MFP to intermediate entities.

or to limit participation in preferred networks to pharmacies willing to accept cost-based reimbursement. PBMs could also use information about a pharmacy's acquisition cost to cut reimbursement for the pharmacy's non-Medicare patients. Such actions would significantly disadvantage community pharmacies. Additionally, because pharmacies may purchase the same medicine from multiple wholesalers, requiring pharmacies to report acquisition costs to wholesalers could also undermine competitive incentives between wholesaler competitors.

Given the issues with acquisition cost detailed above, PhRMA strongly urges CMS to instead define the retrospective MFP discount based on WAC. Using WAC as the pricing benchmark would reduce the risk of creating misaligned incentives for pharmacies and other stakeholders, and any intermediate entity assisting manufacturers in providing access to the MFP would be able to readily determine WAC on the date of dispense, allowing for a seamless, easy calculation of a retrospective MFP discount amount. On average, WAC tends to be a little higher than pharmacy acquisition costs for brand drugs today,⁶⁸ and as such, would best ensure that pharmacies do not incur a shortfall after receiving retrospective reimbursement of an MFP discount and would still allow pharmacies to earn a margin on prescriptions for selected drugs. In contrast, use of acquisition cost, including the National Average Drug Acquisition Cost (NADAC), as a pricing benchmark could significantly reduce or eliminate margins for pharmacies on prescriptions for selected drugs, which could put community pharmacies in particular at risk of closure.

g. Nonduplication with 340B Ceiling Prices (Section 40.4.1)

In section 40.4.1 of the Guidance, CMS states that a Primary Manufacturer is required to provide access to the MFP to 340B CEs if the MFP is below the 340B ceiling price for a selected drug when the CE (or a pharmacy on its behalf, in appropriate cases) dispenses a selected drug to a 340B patient of the CE who is also a Medicare beneficiary. CMS further states that if the 340B ceiling price is "subsequently determined" to be below the MFP, then the manufacturer is responsible for providing the 340B CE the difference between the MFP and 340B ceiling price.

PhRMA has significant concerns that these proposed requirements do not describe the statutory nonduplication clause correctly and conflict with the Agency's proposal in section 40.4 of the Guidance for manufacturers to provide access to the MFP under a retrospective approach by reimbursing pharmacies the difference between the acquisition cost and MFP within 14 days. Specifically, we believe that the Agency's proposed requirements in each section will result in manufacturers providing duplicate MFP and 340B discounts instead of preventing them.

Currently, we understand many CEs manage their 340B inventory virtually using a replenishment model. Under this model, a 340B CE will track, typically with a computerized system, units of medicines dispensed to 340B-eligible patients. When a certain threshold of units is reached, the CE places an order to replenish that stock at the 340B discounted price.⁶⁹ Thus, the medicine is received upfront at the 340B price. This model introduces complexity and is not statutorily mandated.

In such replenishment models, drugs subject to an agreement under section 340B of the Public Health Service Act (340B agreement) are identified after the drug is dispensed. This lag in identification of claims potentially eligible for 340B pricing would make it more difficult to clearly identify whether a 340B discount or MFP discount is owed on a given claim. In addition, it also appears to create an incompatibility with the Agency's proposed requirement for manufacturers to provide pharmacies access to the MFP through a retrospective

⁶⁸ Average pharmacy acquisition costs tend to be 4 percent below WAC based on NADAC data. *See* Myers and Stauffer. (2022). NADAC Equivalency Metrics. Available at: <https://www.medicaid.gov/medicaid/prescription-drugs/downloads/retail-price-survey/nadac-equiv-metrics.pdf>.

⁶⁹ For an overview of the physical inventory model and the replenishment model, as utilized by contract pharmacies in the 340B program, please see: OIG. Memorandum Report: Contract Pharmacy Arrangements in the 340B Program. February 4, 2014. Available at: <https://oig.hhs.gov/oei/reports/oei-05-13-00431.pdf>.

discount equal to the difference between the acquisition cost and the MFP within 14 days, since under the replenishment model, the acquisition cost will vary based on the 340B status of the claim and is not known at the time of dispensing. In other words, a 340B pharmacy using a replenishment model would not know the appropriate acquisition cost in time for manufacturers to meet the proposed 14-day reimbursement requirement. If the pharmacy uses an acquisition cost that is not the 340B price to invoice a manufacturer for a prescription that is later determined to be subject to a 340B agreement, this could result in the manufacturer paying duplicate discounts. And, as noted above, under the IRA's nonduplication clause,⁷⁰ a manufacturer owes nothing further to a CE if the CE already acquired the drug at a 340B ceiling price *lower than* the MFP; it only owes the differential between the 340B ceiling price and the MFP if the CE already acquired the drug at a 340B ceiling price that *exceeds* the MFP.

PhRMA urges CMS, in coordination with the Health Resources and Services Administration (HRSA) to issue clear rules for relevant stakeholders to address this conflict and to prevent duplicate MFP and 340B discounts as required under the IRA. PhRMA recommends the Agency consider several potential solutions:

- *Require identification of 340B units at the point-of-sale.* CMS should require identification of 340B units at the point-of-sale through the use of a claims indicator. This would designate the appropriate acquisition cost, as the 340B status of each prescription would immediately be known and allow manufacturers to be able to pay the retrospective discount to the pharmacy upon appropriate verification from the CE within 14 days.⁷¹ The use of a claims indicator would also align with the requirement for CMS to identify and exclude 340B units from the Part D inflation rebate beginning in 2026.
- *Clarify that manufacturers can choose to make the MFP the “default payment.”* In coordination with HRSA, CMS could require CEs to follow a new retrospective discount mechanism (i.e., a “rebate”) to obtain 340B pricing for selected drugs. CMS should revise the Guidance to state that manufacturers could initially provide the MFP to CEs (or pharmacies dispensing medicines on their behalf) for verified MFP-eligible individuals and then later reimburse CEs for any difference owed between the MFP and the 340B ceiling price (if lower) as a rebate. Under this approach, when invoicing manufacturers, pharmacies or a coordinating intermediate entity would then always use a non-340B acquisition cost for an MFP drug to determine the retrospective MFP discount amount. If it was determined later that a drug was subject to a 340B agreement, and the 340B ceiling price was below the MFP, a manufacturer would reimburse the CE for the difference between the MFP and 340B ceiling price after receiving an invoice from the CE.⁷²

If CMS is not able to address the inconsistency between the proposed Guidance in sections 40.4 and 40.4.1 using one of the solutions outlined above, or another approach, PhRMA urges CMS to withdraw sections 40.4 and 40.4.1 from the revised Guidance to avoid confusion. This would give the Agency additional time to develop a replacement solution to the complicated intersection between 340B and the MFP that works for stakeholders and adheres to the statute's nonduplication clause.

Identifying Units Subject to 340B Agreements

Regardless of the approach CMS chooses to adopt to reconcile the inconsistency between sections 40.4 and 40.4.1 of the Guidance, the accurate identification of units of selected drugs subject to 340B agreements is critical to allowing manufacturers to meet their obligation to provide CEs with the lesser of the MFP or 340B ceiling price

⁷⁰ SSA § 1193(d).

⁷¹ Ibid.

⁷² This proposal should be read consistent with PhRMA's position on the 14-day requirement for providing access to the MFP, as set forth in the preceding section of this comment letter.

when the CE (or a pharmacy on its behalf, in appropriate cases) dispenses a selected drug to a 340B patient of the CE who is also a Medicare beneficiary. Without an accurate way to identify 340B units, manufacturers could be at risk of paying multiple discounts that are meant to be prevented by law.

PhRMA continues to support the Agency’s proposal in the Part D inflation rebate Guidance to require a 340B indicator be included on the PDE record and on all pharmacy claims.⁷³ PhRMA also urges CMS to add a second, “non-340B” indicator value such that the PDE is never silent on the 340B status of each claim. PDE submissions without either of the two indicator values should be rejected as incomplete. This approach would give CMS needed certainty that a 340B determination has been made for each claim. In addition, this would align with the approach taken by the Agency for the discarded drug refund modifier, where providers and suppliers submitting claims for single-dose container or single-use package drugs under Part B must use the “JW” modifier to indicate the amount of a medicine that was discarded, or, effective July 1st, 2023, use the “JZ” modifier to attest that no amount of a medicine was discarded.⁷⁴

Even with a set of mandatory claims indicators, however, PhRMA has significant concerns that all prescriptions subject to a 340B agreement may not be appropriately captured, which could undermine the ability of manufacturers to meet their obligation to provide CEs with the lesser of the MFP or 340B ceiling price when the CE (or a pharmacy on its behalf) dispenses a selected drug to a 340B patient of the CE who is also a Medicare beneficiary. A recent report by IQVIA found that only 61 percent of treatments for Part B separately payable drugs originating at rural referral centers and sole community hospitals used a relevant 340B modifier,⁷⁵ a highly concerning result given that CMS requires these entities to use the “JG” and “TB” modifiers on claims seeking Medicare payment for a 340B-acquired drug. By comparison, IQVIA found that 89 percent of treatments for Part B separately payable drugs originating at disproportionate share hospitals (DSHs) used a relevant modifier.⁷⁶ Since the requirement to use either the “JG” or “TB” modifiers applies equally to DSHs, rural referral centers, and sole community hospitals, the reasons for the significantly different rates of modifier use are unclear.

PhRMA believes that the addition of a “non-340B” indicator value and the rejection of PDE records that lack one of the two relevant values discussed above will help to improve appropriate reporting of units subject to 340B agreements. PhRMA further encourages CMS to establish a robust process to audit 340B CEs to confirm the appropriate identification of units subject to 340B agreements, with penalties for CEs found to be out of compliance. Alternatively, CMS could establish a clearinghouse-type organization to identify 340B units dispensed or administered to Medicare enrollees. The 340B clearinghouse would act as a claims verifier, reviewing Part D PDE data as well as data submitted by 340B CEs (or entities acting on their behalf) to confirm whether a claim is subject to a 340B agreement, similar to the role played by 340B TPAs and split-billing vendors today.⁷⁷ Part D claims identified as being subject to a 340B agreement by either claims indicators or the clearinghouse would then be shared with manufacturers.

Without either a mandate to use a 340B indicator on the PDE or a data clearinghouse that can share identified 340B claims with manufacturers, it is unclear which mechanism manufacturers could use to provide CEs with the lesser of the MFP or 340B ceiling price when a selected drug is dispensed to a 340B patient of the CE who is also

⁷³ CMS. (2023). Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of section 1860D-14B of SSA, and Solicitation of Comments. Available at: <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>

⁷⁴ CMS. (2023). Discarded Drugs and Biologicals – JW Modifier and JZ Modifier Policy: Frequently Asked Questions. Available at: <https://www.cms.gov/medicare/medicare-fee-for-service-payment/hospitaloutpatient/downloads/jw-modifier-faqs.pdf>

⁷⁵ IQVIA. (2023). Can 340B Modifiers Avoid Duplicate Discounts in the IRA? Available at: <https://www.iqvia.com/-/media/iqvia/pdfs/us/white-paper/2023/can-340b-modifiers-avoid-duplicate-discounts-in-the-ira.pdf>.

⁷⁶ Ibid.

⁷⁷ 340B TPAs and split-billing vendors assist 340B CEs in managing prescription 340B eligibility, ordering, and payment. These entities track electronic data feeds (such as inpatient or outpatient status, prescriber eligibility, clinic location, Medicaid payor status, drug identifier, and quantity dispensed) to assess 340B patient eligibility.

a Medicare beneficiary. Thus, it is imperative for CMS to adopt an approach to accurately identify all Part D prescriptions subject to 340B agreements.

II. Negotiation Factors (Section 50)

Sections 50 and 60 of the Guidance describe numerous, closely related elements of the MFP price-setting process (statutory factors, price setting methodology and process, respectively). Overall, CMS' approach to defining the statutory factors in section 50 and Appendix C, as well as the process and methodology described in section 60, falls short of establishing a "consistent process and methodology" for MFP price setting as required in section 1194 of the SSA. To be truly consistent, a methodology must provide a reasonable degree of predictability for stakeholders – particularly manufacturers – on how the factors, and data that underpins them, affect the outcome of the Agency's decision.

Unfortunately, the initial guidance falls short of these standards. The lack of specificity in how individual factors are defined and weighted, combined with an opaque process, results in a subjective and arbitrary price setting framework. We urge CMS to make changes in a revised Guidance to provide needed clarity and specificity in the MFP methodology and factor definition, without resorting to a formulaic approach that does not allow the needed flexibility to account for important clinical differences between medicines and therapeutic areas.

Despite the lack of specificity in the proposed methodology and factor definition, the few details that CMS does articulate almost uniformly point to an approach that will significantly exacerbate the underlying flaws in the statute itself and worsen the impact on patients. Because the IRA directs CMS to "consider" a host of factors, the Agency could balance the factors in a manner that rewards innovation, preserves patient care and advancement, and ensures manufacturers – at a minimum – recoup R&D and costs of production and distribution. Instead, the Agency proposes to:

- Define factors in ways that seem explicitly designed to drive the MFP to excessively low "cost-plus" pricing levels;
- Propose an approach to calculating R&D cost "recoupment" that doubles down on the inherent flaws in the statute's unprecedented inclusion of the concept; and
- Penalize rather than reward manufacturer investments in continued R&D following a drug's approval.

Together, these choices strongly suggest a predisposition to devalue the factors related to the clinical benefits and value of medicines to patients which could help mitigate the law's adverse impact on medical progress. We elaborate on our concerns with CMS' proposed definitions of the statutory factors below. In section III, we discuss concerns with CMS' methodology and process for setting MFPs.

a. Requirements for Submission of Manufacturer Submitted Data Generally (Section 50.1)

In section 50.1 of the Guidance, implementing the "manufacturer-specific data" provisions of IRA (SSA 1194(e)(1)), CMS states that it intends to require that a Primary Manufacturer submit data related to the selected drug to CMS regarding R&D costs of the Primary Manufacturer and whether the Primary Manufacturer has recouped those costs; current unit costs of production and distribution; prior federal financial support for the drug's discovery and development; data on pending and approved patent applications, patent exclusivities, and NDA/BLA approvals; and market data and revenue and sales volume data in the U.S. for the Primary and Secondary Manufacturer. Appendix C of the Guidance includes a list of definitions that describe the data to be collected for the Program.

CMS intends for the Primary Manufacturer to aggregate data from both the Primary Manufacturer and Secondary Manufacturer on the non-FAMP, current unit costs of production and distribution, market data, and revenue and sales volume. It is not workable for Primary Manufacturers to report these data on behalf of Secondary

Manufacturers since Primary Manufacturers likely lack access to such data from Secondary Manufacturers, either legally or practically. See section I, subsection (a) of our comments for our detailed concerns with this part of the Guidance. In addition, as discussed above, there is insufficient time to modify contracts between the parties prior to October 1st, 2023. Further, even if these data were only being collected and submitted by the Primary Manufacturers, we are concerned that the proposed data will be virtually impossible for manufacturers to collect and submit within the 30-day timetable envisioned by the Agency. ***CMS has discretion under the law to permit additional data submission after the October 2nd, 2023 deadline, and we strongly recommend the Agency exercise this discretion.***

Because much of the data required by the IRA are already provided by biopharmaceutical companies under other statutory requirements, CMS should obtain relevant data from publicly available sources wherever possible. For example, ***PhRMA recommends that CMS obtain information about approved patent applications from the FDA's Orange and Purple Book listings and information about approved applications from Drugs@FDA, rather than impose additional burden on manufacturers to submit these data, and companies should be explicitly permitted to reference such sources in their submissions to CMS. Conversely, manufacturers should be permitted to voluntarily provide additional data about manufacturer-specific factors, which could provide necessary context or be helpful to CMS, at their discretion, due to the varied ways in which manufacturers record and maintain information about these factors.*** We note that several areas of the Information Collection Request (ICR) form lack sufficient text limits to allow companies to provide adequate supporting information when companies deem it would be helpful to inform CMS decision-making and should not be constrained in their ability to provide such information. ***PhRMA recommends that CMS amend the Guidance to allow sufficient space for manufacturers to provide a rationale for calculations that approximate spending on manufacturer-specific data elements or have referenced other publicly available information where necessary.***

b. Research and Development (R&D) Costs (Appendix C)

While the statute directs CMS to “consider” R&D costs and the extent to which the manufacturer has recouped such costs, nowhere does the IRA require penalizing biopharmaceutical innovators for recouping R&D, as CMS appears to propose. Indeed, as noted above, the factor could just as easily be read to require a floor, ensuring that, at a minimum, a manufacturer be permitted to recoup R&D. Unfortunately, CMS has chosen to establish standards for the R&D factor that are untethered from the realities of how biopharmaceutical progress occurs, failing to reflect or account for the high-risk nature of research and drug discovery and the complex ecosystem underpinning the U.S. biopharmaceutical research and development enterprise.

CMS also defines the factor in an overly narrow manner, stating that it will review a combination of costs incurred by the Primary Manufacturer for all FDA-approved indications of a drug, such as basic pre-clinical research costs, post-Investigational New Drug (IND) application costs, FDA Phase IV clinical trials, post-marketing trials, abandoned and failed drug costs, and all other R&D costs. CMS proposes to calculate “recoupment” of R&D costs by comparing them to global, total lifetime net revenue for the selected drug. CMS would then increase or decrease the preliminary MFP it calculates depending on whether costs have been “recouped.”

CMS’ proposal to deem that a manufacturer has “recouped” investment based on the global net revenue for the product is fundamentally at odds with maintaining strong incentives for continued R&D. Currently, the biopharmaceutical industry is acknowledged by the Congressional Budget Office (CBO) to be one of the most R&D-intensive in the U.S.⁸⁰ In 2020, U.S. biopharmaceutical R&D investment totaled \$122 billion.⁸¹ Companies invest on average over 20 percent of revenue in R&D,⁸² and in total account for approximately 18 percent of all business-funded R&D in the country, according to data from the National Science Foundation.⁸³ The Brookings Institution reported in 2015 that in 2009 the pharmaceuticals and medicines sector had the highest R&D spending per worker among 50 R&D- and STEM knowledge-intensive industries, at \$143,110. The sector coming in

second on this measure, communications equipment, was more than \$50,000 lower per worker. Even a cutting-edge, high investment sector like semiconductors and other electrical components had R&D spending of only \$49,612.⁷⁸ In sum, the biopharmaceutical industry is the United States' most R&D-intensive sector.

The Agency's flawed approach to assessing "recoupment" of costs reflects a misunderstanding of the economics of the global biopharmaceutical marketplace. Only one of thousands of potential candidates will ultimately result in an FDA-approved medicine, and less than 12 percent of the candidate medicines that make it into Phase I clinical trials are ultimately approved by the FDA.⁷⁶ Following approval, many medicines face significant competition or are not a commercial success.^{77 78} Companies account for these odds when they plan their R&D programs. The revenues from a few successful medicines support continued investment in the high-risk effort to discover new medicines and help to recoup costs of the many failures across their entire portfolio of medicines, not simply, as CMS proposes, those in the same therapeutic class or with the same intended mechanism of action. In sum, because selected drugs are among the subset of medicines with the highest spending in Medicare, they are *by definition* successful and thus likely to have "recouped" their R&D costs by CMS' definition, especially when defined as narrowly as CMS has proposed.

Based on section 60.3.4, CMS appears to be planning to compare global net revenue to R&D costs as defined by CMS to determine whether a manufacturer has recouped its R&D costs. Nowhere does CMS acknowledge that manufacturers necessarily incur a wide range of expenditures, beyond R&D. For instance, manufacturers also must manufacture a drug, incur expenditures to sell a drug in order to earn revenue on it, pay taxes, operate compliance programs, and engage in a variety of other costly operations. Without performing these core functions, a manufacturer would not be in a position to perform R&D. Therefore, CMS' narrow definition greatly overstates revenue that, even in its flawed construct, can reasonably be counted as "recouping" R&D costs.

CMS' definition also ignores ex-U.S. costs necessary to generate global sales. Over the last 20 years the use of multi-regional clinical trials (MRCTs) has become a preferred strategy for rapid new drug development.⁷⁹ MRCTs are conducted in more than one region under a single protocol and allow data generated in one country or region to be leveraged to help gain approval in another country or region. These studies, in addition to clinical trials that may be conducted solely outside the U.S. at the request of regulators, are required for achieving sales in countries around the world and are not necessarily costs related to the U.S. regulatory requirements for INDs or NDA/BLAs. Despite requiring manufacturers to provide the global, total lifetime net revenue from global product sales, CMS' methodology does not explicitly account for these ex-U.S. costs – further increasing the likelihood that manufacturers will be penalized for having "recouped" their costs under CMS' skewed methodology.

All of these concerns reflect the fallacy of CMS' unnecessary interpretation of the IRA, as well as its definitions of costs and "recoupment," both of which will arbitrarily and unnecessarily shift the price down. Given the discretion of the statute (to consider R&D recoupment as a floor, not a downward adjustment), the fact that such downward adjustments could never result in a "fair price," and the economic model that fuels medical advances, CMS should, in specifying "how or to what degree" this factor is applied, state that it will not be used to lower a price determined on the basis of a drug's therapeutic and clinical attributes.

PhRMA recommends that to the extent CMS maintains the flawed proposal on "recoupment," it should place minimal weight on this factor and specify that it will not be used to reduce an MFP determined on the basis of a drug's therapeutic and clinical attributes. Furthermore, the Agency should count only a fraction of global net revenue toward "recoupment" of R&D costs.

⁷⁸ Muro, M., Rothwell J., Andes S., Fikri K., Kulkarni S. (2015). America's Advanced Industries. Brookings Institute. Available at: https://www.brookings.edu/wp-content/uploads/2015/02/AdvancedIndustry_FinalFeb2lores-1.pdf.

Finally, CMS' approach to implementing this aspect of the statute is not only at odds with the way that manufacturers operate and invest in R&D, but also creates significant burden and complexity. In most cases it will be extremely challenging for manufacturers to quantify costs as required by CMS – and will be virtually impossible to comply within the 30-day timeframe. CMS has requested that manufacturers provide the costs of direct and indirect basic pre-clinical research costs on drugs with the same active moiety/active ingredient or mechanism of action as the selected drug that did not make it to clinical trials. This will require companies to produce a record of costs incurred for pre-clinical data that may be 20 or more years old, a herculean task. For companies with ex-U.S. headquarters, global data may not be easily accessible, or accessible at all, in the normal course of business to U.S. affiliates. In addition, pre-clinical costs may include, for example, investments in platform technologies that are used across multiple drug development programs, as well as development tools such as model-informed drug development or AI programs. As a result, calculation of product-specific R&D will require allocation of costs across drug development programs and products at the level of granularity which is prescribed in the guidance. Similarly, costs for “abandoned and failed” products may be difficult if not impossible to attribute to a drug development program in the ways CMS has specified. These difficulties are compounded when drug products are developed through the efforts of multiple companies, through early-stage R&D licensing arrangements, or other partnerships.

We urge CMS to recognize total investments across the entire portfolio. Rather than creating requirements that are virtually impossible for companies to accurately comply with, CMS should provide manufacturers with flexibility to provide information on broader R&D costs, including information about pre-clinical costs, failed and abandoned drug costs as well as “other R&D costs.” Other costs may include costs of global development and regulatory submission activities. Companies should also be permitted to rely on benchmark/industry-wide data in cases where a company may not maintain the data itself.

CMS should amend the Guidance to limit required submission of R&D costs to data available to the manufacturer that can be directly attributable to the selected drug, while allowing companies to voluntarily provide supplemental data. In addition, manufacturers should be given the opportunity to provide a supporting narrative.

c. Current Unit Costs of Production and Distribution (Appendix C)

Regarding current unit costs of production and distribution, CMS would define costs of production to include all direct and indirect costs related to purchasing raw ingredients, including intermediates, active pharmaceutical ingredients, excipients, and other bulk chemicals; formulating and preparing the finished drug product; performing quality control and testing of the drug; and operating costs for personnel, facilities, transportation, any importation, and other expenses related to preparing the finished drug product. Distribution costs would include all direct and indirect costs related to packaging and materials; labeling; shipping to any entity that acquires the drug from the Primary or Secondary Manufacturer; and operating costs for any of the above. Current unit costs would include only costs incurred by the Primary and Secondary Manufacturer and only units produced and distributed for sale in the U.S. R&D costs and marketing costs would not be included.

CMS' proposed definition for the unit costs of production and distribution in the Guidance is concerning. CMS has expanded the language on this factor beyond the statute to a level of additional detail and specificity that companies may not have access to, particularly in situations where companies may be working with additional suppliers and manufacturers in the supply chain. ***PhRMA strongly recommends that rather than specifying the definition, CMS allow discretion for manufacturers to describe production and distribution costs which they are able to report and to provide a narrative explanation describing how these costs were calculated.***

d. Prior Federal Financial Support (Appendix C)

CMS would define prior federal financial support to include tax credits, direct financial support, grants or contracts, and any other funds provided by the federal government to support discovery, research, and/or development of the selected drug – all during the time period from when initial research began or when the drug was acquired by the Primary Manufacturer, through the date the most recent NDA/BLA was approved. CMS states that it may consider decreasing the preliminary price if funding for the drug’s discovery and development was received with federal financial support.

PhRMA is disappointed with CMS’ decision to broadly define federal financial support and strongly disagrees with the notion that tax credits, including orphan drug tax credits, are appropriate for inclusion as “prior federal financial support,” which would serve to undermine the incentive that the credits are intended to provide by decreasing a selected drug’s MFP. Tax credits serve to incentivize R&D spending on life-saving medicines and, for orphan drugs, that spending is for medicines for rare diseases. These tax credits are critical to incentivize innovation and are not akin to the government providing direct support to a company’s research efforts and CMS’ policy undermines longstanding intent by Congress to incentivize R&D into these difficult to treat diseases.

PhRMA urges CMS to remove tax credits from the definition of “prior federal financial support.”

America’s biopharmaceutical industry is at the heart of a robust R&D ecosystem that develops more innovative drugs than any other country in the world. The industry’s unique role in that ecosystem is to utilize its scientific and industrial expertise to take the necessary risks to build upon and further advance basic science research into safe and effective treatments that can be made available to patients. Private sector companies regularly fund academic researchers and collaborate with government-funded scientists to advance a variety of promising scientific concepts to better understand various disease states and drug targets. However, many of those explorations are not ultimately included in developing the actual products for patient use. Rather, this knowledge must be shared and further expanded upon to contribute to potential new drugs and drug targets. ***Therefore, PhRMA recommends that CMS limit its consideration of prior federal financial support for discovery and development solely to funding that resulted in a patent application containing a Government Interest Statement and/or research where a patent assignee was a U.S. government agency for an invention directly related to the development of the selected drug (e.g., excluding basic science, research tools, or similar general concepts). PhRMA also requests that CMS clarify that prior federal financial support needs to be reported only for the time period starting when the Primary Manufacturer acquired the drug, even where this approach may result in the reporting of no prior federal financial support during the relevant period for products associated with patent applications that included a government interest statement.***

e. Patents, Exclusivities, and Approvals (Appendix C)

Regarding patents, exclusivities, and approvals, CMS considers relevant patents to be those that are pending or approved and linked to the selected drug as of September 1st, 2023, as well as pending and approved applications for which a claim of patent infringement could reasonably be asserted against a person engaged in the unlicensed manufacture, use, or sale of the selected drug. CMS notes that FDA exclusivity periods include Orphan Drug Exclusivity and Pediatric Exclusivity. CMS states that it will consider the length of the available patents and exclusivities before the selected drug may no longer be single source and may consider decreasing the preliminary price if the selected drug has patents and exclusivities that will last for a number of years.

PhRMA strongly disagrees with CMS’ proposal to decrease the MFP for selected drugs that have remaining patents and exclusivities. Instead, we recommend CMS take the opposite approach and recognize the benefit provided by these investments and consider adjusting the preliminary price upward based on these protections. Patent rights are a form of intellectual property (IP) protection enunciated in the U.S. Constitution and are critical to the continued investment in R&D, including for new medicines and improvements for existing medicines. Patents require the description of inventions to be disclosed to the public, allowing society to understand and learn from the invention, and this disclosure lays the groundwork for competition from nonidentical drugs that treat the

same conditions as well from generics and biosimilars. Annualized savings from biosimilars reached \$6.5 billion in 2020, and competition from generics and biosimilars is expected to reduce U.S. brand sales by \$128 billion through 2025.⁷⁹

CMS' proposal to penalize manufacturers for the lengthy, costly, and risky R&D that has resulted in new innovations protected by patents and exclusivities will undermine U.S. leadership in biopharmaceutical innovation and weaken the intent of the IP system. As a matter of course, drugs selected for price setting at 7 or 11 years will have remaining patents and exclusivities, which may include, for example, unexpired 7-year orphan-drug exclusivity for an orphan indication approved after the drug's initial approval or a 3-year new clinical exclusivity earned through new clinical trials of a drug product. Indeed, as a matter of law, innovative biologics receive 12 years of exclusivity following first licensure, and pediatric exclusivity would extend this period another six months. Thus, CMS' policy choice of penalizing patents and exclusivities would broadly undercut incentives for progress.

In addition, manufacturers should not be penalized in cases where they have obtained patents and exclusivities for innovation, including for important advances and improvements made after an initial FDA approval. Patents and exclusivities covering post-approval innovations may not affect the timing of approval and launch of generic or biosimilar products that omit a new indication, do not seek approval of an improved formulation, or are not made using a more efficient manufacturing process. It would be unjust to penalize manufacturers for obtaining patents and exclusivities that do not extend the single-source status of a product. Additionally, by choosing to adopt a policy of reducing the MFP from the ceiling price due to the existence of remaining patents and exclusivities, CMS would eviscerate these incentives that Congress created to promote innovation, knowledge-sharing, and benefits to patients and society. For example, existing incentives in the Best Pharmaceuticals for Children Act to conduct pediatric development beyond any required pediatric studies would be weakened. Actions related to patents should be left to legislation and where appropriate, the proper administrative body, i.e., USPTO. There is no indication that Congress intended for the IRA to hollow out these incentives in the manner that CMS proposes. Indeed, by imposing a financial penalty on manufacturers for obtaining patents and exclusivities, CMS would exacerbate the serious concerns that the Program raises under the Takings Clause of the Fifth Amendment to the U.S. Constitution, including by effectively depriving manufacturers of part of the value of a patent or exclusivity.⁸⁰

Post-approval R&D often results in innovations that can improve patients' lives. In fact, more than 60 percent of oncology medicines approved a decade ago received approvals for additional indications in later years, and most of those occurred seven or more years after initial FDA approval. Such post approval research often requires lengthy and costly clinical trials, taking a total of three to six years. Penalizing manufacturers for both patents and/or exclusivities on the original product as well as post-approval innovations would fundamentally change incentives for improving patient and doctor choice as well as continued investment in research following a drug's initial approval. Perversely, CMS' proposed policy would penalize the development of the very attributes of medicines and knowledge about medicines' performance that CMS states it will evaluate under the elements of this Guidance related to assessing a drug on its clinical dimensions. Indeed, the statutory classification of a selected drug as a short-monopoly drug, extended-monopoly drug, or long-monopoly drug already provides a mechanism for reducing the ceiling price and renegotiating the MFP as additional years elapse since approval. CMS should not further penalize manufacturers in the manner described in the guidance. ***PhRMA urges CMS to amend the Guidance and clarify that if a drug has existing unexpired patents or exclusivities, rather than penalizing the manufacturer with a lower price, it should result in an upward shift of the preliminary price to reflect the innovation in the product.***

⁷⁹ IQVIA Institute Report (2020). Biosimilars in the United States 2020 – 2024.

⁸⁰ U.S. Const., Amend. V.

Regarding submission of information on pending or approved patent applications, ***PhRMA suggests that CMS consult the FDA’s Orange and Purple Book listings, as well as provide flexibility for manufacturers to supplement these listings to provide information about pending patent applications and other relevant facts.*** CMS should not use information about pending patent applications to adjust its preliminary price downward. Claims for infringement cannot be based on a pending application, and it would be premature to decide about the exclusionary effect of a patent application before issuance of a patent because the claims can change significantly during prosecution and a patent ultimately might not be granted. Also, CMS should explicitly confirm that “pending applications” for submissions purposes do not include abandoned applications, which would not be relevant for CMS’ price-setting process and are considered neither pending nor approved patent applications. CMS should further clarify that manufacturers are not required to submit non-public patent information, including information about pending applications that have not been published, given the highly confidential nature of this information. Manufacturers should also be permitted to refer CMS to the Orange and Purple Book for exclusivity data and Drugs@FDA for information about approved applications. Manufacturers could then supplement those sources with information about pending applications.

In addition, the definition of relevant patent information to include pending and approved patent applications “relating to the selected drug” and patents “linked to the selected drug” is vague and could encompass patents and patent applications that have no bearing on the continued single-source status of a selected drug.⁸¹ For example, it could entail the submission of information about foreign patents and patent applications, as well as patents that are neither owned nor licensed by the Primary Manufacturer. The reference to “patents linked to the selected drug where the Primary Manufacturer is not listed as the assignee/applicant,” in particular, is inconsistent with the statutory requirement that the manufacturer submit “[d]ata on pending and approved patent applications . . . for the drug.”⁸² Moreover, it is unclear how the scope of relevant patent information defined in the Guidance aligns with the statutory standard for the listing of patent information in the Orange Book.⁸³ ***CMS should only consider patents and patent applications that are directly related to the selected drug, as opposed to those directed to basic science, research tools, and similar general concepts, manufacturing processes, unapproved uses, unapproved formulations and dosage forms, metabolites, intermediates, and third-party patents and applications for which the manufacturer has no rights of enforcement.*** CMS should only require information about patents and patent applications that is relevant to whether a selected drug will remain single source. CMS should provide a standard for relevance that is consistent with the scope of the requirement to submit patent information for listing in the Orange Book and Purple Book.

f. Market Data and Revenue and Sales Volume Data (Appendix C)

CMS proposes to require that manufacturers report more than 20 metrics relating to drug prices and sales under “Market Data and Revenue and Sales Volume Data” (see Appendix C): WAC unit price; National Council for Prescription Drug Programs (NCPDP) billing unit standards; 340B ceiling price; Medicaid Best Price; AMP; 340B prime vendor program price; Federal supply schedule (FSS) price; Big Four price; U.S. commercial average net unit price, with and without patient assistance and “best”; manufacturer average net unit price to Part D Plan sponsors with and without patient assistance and “best”; total U.S. gross revenue; total U.S. net revenue with and without patient assistance; and quarterly total U.S. unit volume. In most cases CMS would require the Primary Manufacturer to aggregate its own data on the selected drug from both the Primary Manufacturer and data from

⁸¹ Guidance at 88.

⁸² SSA § 1194(e)(1)(D).

⁸³ See Federal Food, Drug, and Cosmetic Act § 505(b)(1) (requiring the submission of patent information for “any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.”).

any Secondary Manufacturer. The Guidance specifies that all of these data with explanations must be submitted to CMS within 30 days of selection – by October 2nd, 2023.

PhRMA has major concerns with these reporting requirements specified as “Market Data and Revenue and Sales Volume Data.” These requirements are extremely broad and would impose substantial burdens on manufacturers, especially given the short time period to collect the data and the need to gather data from all Secondary Manufacturers. As discussed in response to section 40, it would be legally problematic and extremely challenging for Primary Manufacturers to gather the vast amounts of data CMS is asking them to collect from Secondary Manufacturers. CMS fails to provide any justification or rationale for the breadth of this proposed data requirement. The Guidance also introduces two new pricing metrics (each with three variations) with little explanation as to which sales and discounts should be included in and excluded from these calculations. Manufacturers are required to report a new “U.S. commercial average net unit price” in three ways (with patient assistance programs, without patient assistance programs, and “best” price) and a “manufacturer average net unit price to Part D Plan sponsors” similarly (with patient assistance programs, without patient assistance programs, and “best” price).

CMS unjustifiably fails to define these new metrics with specificity or any reference to existing terms or rules, which is a marked departure from how Congress and agencies have defined pricing metrics and calculations in other federal drug pricing programs such as the Medicaid Drug Rebate Program, the 340B Drug Pricing Program, the Federal Ceiling Price statute and related U.S. Department of Veterans Affairs (VA) guidance, and the FSS. In doing so, CMS fails to grasp the potential for the lack of clear definitions to cause inconsistency in the way these metrics are reported and calculated, and thus what meaning they may have. Without additional CMS guidance, these metrics would pose considerable risk to manufacturers, who will be required to report in a compressed timeframe under the serious threat of CMPs. Moreover, the new reporting requirements, if finalized, would place unnecessary burdens on manufacturers given that a significant portion of this information is already reported to and available to CMS such as net prices to Part D and Medicaid Best Price.

To help address such gaps in reporting instructions, manufacturers would have to develop a set of reasonable assumptions to calculate these various new metrics and then rely on these assumptions to report these metrics. Yet the Guidance increases the risk of nonuniform and perhaps unintentionally inaccurate reporting in multiple ways, including the following:

- The Guidance makes flawed assumptions about manufacturer patient assistance, requiring that manufacturers calculate and report new metrics with and without patient assistance (“U.S. commercial average net unit price,” with and without patient assistance; “manufacturer average net unit price to Part D Plan sponsors” with and without patient assistance; and “total U.S. net revenue” with and without patient assistance). Patient assistance is financial assistance intended to reduce patients’ out of pocket costs and is not considered a price concession offered to customers.⁸⁴ In other words, patient assistance does not constitute “market” data under SSA § 1194(e)(1). But this is the rubric under which CMS would require manufacturers of selected drugs to report their patient assistance amounts.
- Moreover, the Guidance would require manufacturers to calculate and report a Part D price (“manufacturer average net unit price to Part D Plan sponsors”) “with patient assistance” when the

⁸⁴ See, e.g., 42 CFR § 447.505(c)(8)-(12)(CFR as of December 31, 2020) (excluding from Medicaid Best Price specified types of patient assistance, to the extent the benefits were not provided to other parties, regulations that were revised by a December 31, 2020 “accumulator adjustment rule” that was itself overturned in court); *PhRMA v. Becerra*, 2022 WL 1551924, *5 (D.D.C. 2022)(overturning the “accumulator adjustment rule” that would have generally resulted in manufacturers having to include patient assistance in their Best Price determinations, and emphasizing that “A manufacturer’s financial assistance to a patient does not qualify as a price made available from a manufacturer to a best-price-eligible purchaser. Rather, a manufacturer’s financial assistance is available from the manufacturer to the patient”).

federal anti-kickback statute would generally prohibit them from offering cost-sharing assistance to Part D patients, and when patient assistance is not given to or intended for any type of “plan sponsors” – all of which raises further questions and confusion about what CMS even means by “patient assistance” and thus how manufacturers could reasonably interpret and carry out these new reporting mandates.

- A closely related source of confusion and uncertainty – and risk--- is that the Guidance is silent on whether a “patient assistance program” is meant to include a manufacturer’s charitable free drug programs (which it should not). The fact that CMS refers to “patient assistance” in a Part D context where manufacturers do not provide cost-sharing assistance to patients causes further questions about what CMS means by “patient assistance.” Yet there is language in the data elements ICR that seems to consider only “coupons and copay assistance” as the patient assistance that CMS is asking manufacturers to report.⁸⁵

To correct these problems, CMS should withdraw all of the new metrics. Failing that, CMS should delete all items asking for manufacturers to report “patient assistance” from the Guidance (and the related data elements ICR). If any references to patient assistance are retained, we ask that CMS define what constitutes a “patient assistance program” and explicitly clarify that a “patient assistance program” does not include manufacturer charitable free drug programs.

It might appear initially that manufacturers of selected drugs could resolve all of these problems by adopting appropriate reasonable assumptions and specifying these assumptions in their data reports to CMS. But manufacturers are being required to develop their reasonable assumptions, perform and test their calculations, and report this information to CMS – in some cases all while collecting and seemingly blending in data from one or more Secondary Manufacturers, plus with caps on the amount of text they can provide in their narratives explaining their reported data to CMS – in a time frame that is impracticable, and at risk of severe penalties for submitting data that CMS ultimately deems insufficient or inaccurate.⁸⁶ These burdensome procedures are in no way necessary for CMS to make MFP determinations and accordingly we urge CMS to rectify these problems when revising its Guidance.

Finally, PhRMA takes issue with how CMS plans to use the market and sales data during the price setting process. For example, according to section 60.3.4 of the Guidance, if one of the new metrics reported – e.g., “average commercial net price – is lower than the “preliminary price,” CMS may adjust the preliminary price downward. Yet CMS provides no explanation for the relationship between these prices, or for why a lower commercial net price (or any of these pricing metrics) should drive the preliminary price down, and likely result in a lower MFP.⁸⁷

CMS should at a minimum withdraw these new metrics (i.e., all three variations of “U.S. commercial average net unit price” and “manufacturer average net unit price to Part D plan sponsors, respectively) in the revised Guidance. In the revised Guidance CMS should only require reporting of existing price reporting metrics (e.g., WAC, AMP). It is also critical that CMS permit manufacturers to submit all of the market and sales data under a reasonable timeframe (and in particular beyond October 2nd, 2023, which we believe the statute permits), and without limits on the number of lines or words manufacturers can use to explain their assumptions or other aspects of their metrics.

⁸⁵ ICR for Negotiation Data Elements under sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW) Questions 31-36, p. 33-37.

⁸⁶ Id. The ICR limits manufacturer responses explaining their reported pricing data and reasonable assumptions to a free text box that has a “1,000 word limit.” P. 35-36.

⁸⁷ Guidance, p. 53.

g. Quality-Adjusted Life Years (QALY) and Cost Effectiveness Analysis (Section 50.2)

PhRMA appreciates CMS' acknowledgement that it will not use quality-adjusted life years, or QALYs, in its determination of MFPs for selected drugs in a "life-extension context," given their discriminatory nature and failure to accurately capture the benefits treatments offer to patients. (CMS does not define "life extension context" in the Guidance document.) While we agree with CMS' statement that the language set forth in the IRA prohibits CMS' reliance on QALYs or similar metrics, we are concerned that CMS overlooks a separate, but equally relevant prohibition on reliance on QALYs that is more broadly applicable across Medicare that was enacted as part of the Affordable Care Act.

Specifically, CMS fails to reference the existing prohibition on Medicare reliance on QALYs or similar metrics found in the SSA.⁸⁸ This prohibition would prevent CMS from using QALYs as part of its determination of MFPs, including in a "life extension context", including in CMS' determinations of MFPs. ***PhRMA recommends CMS explicitly acknowledge this additional statutory prohibition in its revised Guidance, and refrain from using QALYs or any similar metric, in any context.*** Given the concerns of numerous stakeholders regarding use of QALYs and similar metrics, clarity and transparency in this matter is absolutely critical as CMS implements the Program. By clearly and unequivocally precluding these standards from MFP decision-making, CMS will build trust with stakeholders and the public at large.

It is widely acknowledged that QALYs, which are the basis for many cost effectiveness analyses (CEA), discriminate against seniors, the disabled, communities of color, and the chronically ill. As noted by the National Council on Disability, "QALYs place a lower value on treatments which extend the lives of people with chronic illnesses and disabilities."⁸⁹ These concerns have been echoed repeatedly by numerous stakeholders – in 2021, more than 80 stakeholder groups signed a letter led by the American Association of Persons with Disabilities, "strongly urging policymakers to reject potentially catastrophic legislation and policies that reference QALYs and similar metrics."⁹⁰ Even leading academics who have long relied upon QALYs for their work, have acknowledged that "the problem of whether [QALYs] unjustly discriminate[s] against the disabled remains a deep and unresolved difficulty."⁹¹

PhRMA also strongly recommends that CMS commit to avoiding reliance on CEAs, regardless of the metric it is rooted in, when determining a selected drug's MFP as part of this process. Reliance on CEA, whether it is rooted in QALYs or another similar metric, as the basis for policy decisions risks further discriminating against underserved and underrepresented people of color who are already at higher risk of not receiving the care they need. Given CMS' priority to improve health equity, this should be of particular concern. According to Tufts Medical Center, fewer than five percent of CEAs stratify results by race or ethnicity.⁹² And because CEA ignores important patient differences in communities of color – such as differences in treatment, disease risk, health status, or life expectancy – it ignores (and potentially worsens) systemic inequities that harm people in those communities. For example, as Black seniors are more likely to die of colon cancer,⁹³ some treatments have been

⁸⁸ SSA § 1182(e).

⁸⁹ National Council on Disability. (2021). NCD Letter to Congress recommending QALY ban in Build Back Better Act. Available at: <https://ncd.gov/publications/2021/ncd-letter-qaly-ban>.

⁹⁰ American Association of People with Disabilities. (2021). "Reject Health Policies that Discriminate." Available at: <https://www.aapd.com/wp-content/uploads/2021/04/Reject-Health-Policies-that-Discriminate-1.pdf>.

⁹¹ Neumann P, Sanders G, et al. (2017). Cost Effectiveness in Health and Medicine, Second Edition.

⁹² Lavelle TA, Kent DM, Lundquist CM, Thorat T, Cohen JT, Wong JB, Olchanski N, Neumann PJ. (2018). Patient Variability Seldom Assessed in Cost-effectiveness Studies. Med Decis Making. 38(4):487-494. DOI: 10.1177/0272989X17746989. Epub 2018 Jan 19. PMID: 29351053; PMCID: PMC6882686.

⁹³ Office of Minority Health. (2021). "Cancer and African Americans." Available at: <https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=16>.

estimated to be more effective in improving survival among Black patients relative to other races.⁹⁴ CEA, which determines what works for an average patient population, would obfuscate the value of treatments to Black patients.

QALY-based CEA also often assigns a lower value to Black lives. Researchers found that the life of a Black patient with diabetes and visual impairment is valued as having 15 percent fewer QALYs remaining compared to White patients with the same diseases.⁹⁵ Additionally, QALY-based research systematically undervalues communities of color because they have lower life expectancy relative to the average population⁹⁶ due to factors including worse access to care,⁹⁷ lower quality of care,⁹⁸ and higher risk of disease.⁹⁹ As a result of shorter life expectancies, Black patients' lives would be automatically valued ten percent less than White patients.¹⁰⁰

CEA based on any metric can present significant concerns beyond those issues related to discrimination, as it often fails to capture benefits and impacts that matter to patients or patient subgroups. For example, generic measures, such as the EQ-5D, are often used for capturing patients' health-related quality of life to assess QALYs.¹⁰¹ While these types of measures are useful for simplifying the comparison of different interventions, they do not always capture all the dimensions of quality of life that are important to patients. For example, researchers have noted that the EQ-5D may fail to reflect the entirety of quality of life for patients with sickle cell disease by not including domains such as fatigue, stigma, fluctuations in pain (particularly from recurrent painful vaso-occlusive events or pain crises), or the impact of racial disparities all of which are relevant for people with sickle cell disease.^{102,103}

We caution against use of metrics that seek to address the discriminatory nature of QALYs, but have their own flaws. In addition to documented equity and technical issues, these measures have been shown to inaccurately and incompletely capture the full impact of treatments on patients. For example, in response to the controversy surrounding QALYs, the Institute for Clinical and Economic Review (ICER) developed a new metric for quantifying value, the equal-value life year gained (evLYG).¹⁰⁴ However, the evLYG introduces new problems. For example, the evLYG devalues drugs for conditions that do not extend life expectancy, like eczema or blindness, so therapies for these conditions would be seen as having no value.¹⁰⁵ Thus, the evLYG would value

⁹⁴ Mack CD, Carpenter W, Meyer A, Sanoff H, Stürmer T. (2012). "Racial Disparities in Receipt and Comparative Effectiveness of Oxaliplatin for Stage III Colon Cancer in Older Adults." Available at: <https://acsjournals.onlinelibrary.wiley.com/doi/pdfdirect/10.1002/cncr.26622>.

⁹⁵ McCollister K, Zheng DD, Fernandez CA, Lee DJ, Lam BL, Arheart KL, Galor A, Ocasio M, Muennig P. (2012). "Racial Disparities in Quality-Adjusted Life-Years Associated with Diabetes and Visual Impairment. *Diabetes Care*. 35; 1692-1694. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3402250/pdf/1692.pdf>.

⁹⁶ Arias E, Tejada-Vera B, Ahmad F, Kochanek KD. (2021). "Provisional Life Expectancy Estimates for 2020." *Vital Statistics Rapid Release*. Available at: <https://www.cdc.gov/nchs/data/vsrr/vsrr015-508.pdf>.

⁹⁷ Centers for Disease Control and Prevention. (2021). "Health Equity Considerations and Racial and Ethnic Minority Groups." Available at: <https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/race-ethnicity.html>.

⁹⁸ Broder M., Ortendahl J. (2021). "Is Cost-Effectiveness Analysis Racist?" PHAR. Available at: <https://blogsite.healtheconomics.com/2021/08/is-cost-effectiveness-analysis-racist/>.

⁹⁹ Office of Minority Health. (2018). "Minority Population Profiles." Available at: <https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=26>.

¹⁰⁰ Broder M., Ortendahl J. (2021). "Is Cost-Effectiveness Analysis Racist?" PHAR. Available at: <https://blogsite.healtheconomics.com/2021/08/is-cost-effectiveness-analysis-racist/>.

¹⁰¹ Mott, D., Kumar, G., Sampson, C., Garau, M. (2021) How is Quality of Life Measured for Health Technology Assessments? Office of Health Economics. Available at: <https://www.ohe.org/publications/how-quality-life-measured-health-technology-assessments>.

¹⁰² Mott, D., Garau, M. (2022). When Generic Measures Fail to Reflect What Matters to Patients: Three Case Studies. Office of Health Economics. Available at: <https://www.ohe.org/publications/when-generic-measures-fail-reflect-what-matters-patients-three-case-studies#>.

¹⁰³ Power-Hays, A., McGann, P. T. (2020). When Actions Speak Louder than Words – Racism and Sickle Cell Disease. *N Engl J Med*; 383:1902-1903.DOI: 10.1056/NEJMp2022125.

¹⁰⁴ ICER. (2018). "The QALY: Rewarding the Care that Most Improves Patients' Lives. Available at: https://icer.org/wp-content/uploads/2020/12/QALY_evLYG_FINAL.pdf.

¹⁰⁵ Cohen JT, Ollendorf, DA, Neumann PJ. (2018). "Will ICER's Response to Attacks on the QALY Quiet the Critics?" Tufts Center for the Evaluation of Value and Risk in Health. Available at: <https://cevr.tuftsmedicalcenter.org/news/2018/will-icers-response-to-attacks-on-the-qaly-quiet-the-critics>.

two drugs, one that reduces side effects and one that does not, as of equal value, even though side effects have a significant impact to patients. Neither the QALY nor the evLYG properly captures the value of a drug to patients and people with disabilities, and CMS should avoid reliance on either.

Furthermore, PhRMA has significant concerns about how CMS intends to implement the statutory prohibition on use of QALYs and similar metrics, critical to protecting patients and persons with disabilities, many of whom strongly oppose these standards. In the Guidance, CMS states that in situations where a study uses QALYs but also has “clearly separated” this use from other evidence in the study that is relevant to the price-setting factors, CMS will consider this “separate evidence.” CMS also notes that it will “ask” entities to state whether or not the research submitted contains QALYs, thus placing the responsibility entirely on CMS to ensure that QALY-based research is not considered in determining MFPs for selected drug. Beyond those statements there is a worrisome lack of specifics offered as to how CMS intends to operationalize and enforce the QALY prohibition. When combined with the overall lack of transparency in CMS’ decision making, this proposal is likely to erode public trust in the program.

As it stands, CMS does not have the time and expertise to review large quantities of data and separate out the information in the study that is relevant to the price-setting factors but does not implicate the use of QALYs. Further, CMS fails to define “clearly separated” sufficiently to allow stakeholders to understand what information is prohibited and what is not. It is unclear to what degree any influence QALY-based research has on other parts of research that are not QALY-based automatically disqualifies the non-QALY based research from consideration. Instead of allowing CMS to judge the separation, CMS should require that entities submitting information have removed QALY-based information. Often, non-QALY driven comparative effectiveness research is not easily cleaved from its QALY-based parts. ***PhRMA recommends that CMS require that any entity submitting information attest to having removed QALY (or similar metric)-based research from its submission.***

h. Standards for Review of Literature and Research (Section 50.2)

In describing the approach it will take to determining MFPs for selected drugs, CMS states that it intends to review existing literature and real-world evidence (RWE). In a single sentence, CMS also describes criteria it may consider in determining the literature it intends to review as part of setting MFPs. While PhRMA appreciates CMS offering these criteria, we believe that this falls far short of what is necessary to ensure that the evidence CMS relies upon is fit for purpose. For example, CMS states that it will consider “rigor of the study methodology” but does not describe what qualifies as methodologically rigorous or cite examples of third-party standards that evidence must meet to be considered.

Failure to provide clarity around the quality and characteristics of evidence CMS intends to consider will undoubtedly undermine CMS’ methodology for setting prices in the eyes of manufacturers and other stakeholders, and deprive manufacturers of necessary predictability in terms of how CMS will arrive at MFPs. Therefore, ***PhRMA recommends that CMS go several steps further, and develop robust standards it will adhere to ensure that the evidence it both relies upon and develops is methodologically rigorous and patient-centered.*** The development of such standards is critical to giving manufacturers, as well as other stakeholders, confidence in the research CMS develops and relies upon in determining MFPs.

Standards for quality and patient-centeredness are not only critical for third-party evidence reviewed by CMS, but for CMS’ internal analysis as well. CMS notes in section 50.2 that in addition to reviewing existing literature, it will also “conduct internal analytics”, though it does not provide further detail on what those analytics might entail. It also does not appear from the Guidance that CMS intends to apply the aforementioned criteria to its own analysis, which is concerning. It is not only critical that external evidence CMS considers be methodologically rigorous and patient-centered, but that CMS’ own analyses achieve these goals. Therefore, ***PhRMA recommends that CMS clarify that its own internal analytics will be required to meet well-defined quality standards as well.***

There is a significant body of work that CMS may choose to borrow from in developing standards for rigor and patient-centeredness. Several organizations have done work to create best practices, guiding principles and guidelines in establishing principles and standards for evidence and data. CMS should pay particular attention to the standards set forth by patient advocacy organizations such as the National Health Council, which have also developed their own guidance in evaluating the quality and patient-centeredness of value assessment frameworks.¹⁰⁶ The National Health Council has developed a rubric for Patient Centered Value Assessment,¹⁰⁷ which outlines six key domains¹⁰⁸ that PhRMA agrees are critical to ensuring the evidence and organizations CMS relies upon in determining a selected drug's MFP are of high-quality and are patient-centered. The rubric also contains additional details on specific domains that CMS should reference when developing its own standards.

CMS should look to academically driven organizations as well. For example, the International Society for Pharmacoepidemiology (ISPE) created “Guidelines for Good Pharmacoepidemiology Practices (GPP),” which propose essential practices and procedures that should be considered to help ensure the quality and integrity of pharmacoepidemiologic research, and to provide adequate documentation of research methods and results.¹⁰⁹ While adherence to these guidelines does not ensure valid or robust research, they provide a starting point in achieving a methodologically sound framework for the research and data CMS plans to both conduct and review as part of MFP setting.

PhRMA has public, well-established principles¹¹⁰ on evidence-based medicine and value assessment that reflect the consensus and knowledge of experts in the biopharmaceutical industry. While these best practices focus on value assessment in the context of private sector decision-making, there is still significant relevance in their content. The National Pharmaceutical Council also has detailed guiding practices for value assessment.¹¹¹

Academics and researchers such as the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Special Task Force on U.S. Value Assessment Frameworks have established best practices for health technology assessments (HTA). While the Task Force recommendations extend beyond the scope of review established in the IRA (e.g., by making recommendations related to cost-effectiveness analysis), they do illustrate the importance of CMS considering a broad range of value elements (e.g., fear of contagion, scientific spillover).

i. Standards for Third Parties Conducting Technology Assessments (Section 50.2)

CMS also notes that it will “consult subject matter experts as part of its process to set MFPs for selected drugs, in addition to considering evidence from “the Primary Manufacturer and members of the public, including other manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested parties.” However, CMS has thus far failed to provide any information to the public about what third-party evidence it will rely upon in making MFP determinations. Building on our recommendation above that CMS create robust standards for the evidence it will consider in determining MFPs (as discussed above), *PhRMA recommends CMS set standards in*

¹⁰⁶ National Health Council. (2021). Value Classroom. Available at: <https://nationalhealthcouncil.org/education/value-classroom/>.

¹⁰⁷ National Health Council. (2016). The Patient Voice in Value: The National Health Council Patient-Centered Value Model Rubric. Available at: <https://nationalhealthcouncil.org/wp-content/uploads/2020/11/20160328-NHC-Value-Model-Rubric-final.pdf>.

¹⁰⁸ These domains include: (1) Patient Partnership, (2) Transparency to Patients, (3) Inclusiveness of Patients, (4) Diversity of Patients/Populations, (5) Outcomes Patients Care About, (6) Patient-Centered Data Sources. Learn more at: https://nationalhealthcouncil.org/wp-content/uploads/2020/03/NHC-One-Pagers_Domains.pdf.

¹⁰⁹ Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making, available at: <https://www.ispor.org/docs/default-source/publications/newsletter/rwe-data-treatment-comparative-effectiveness-guideline.pdf>.

¹¹⁰ PhRMA. (2016). Principles for Value Assessment Frameworks. Available at: <https://phrma.org/resource-center/Topics/Cost-and-Value/Principles-for-Value-Assessment-Frameworks>.

¹¹¹ National Pharmaceutical Council. (2016). Guiding Practices for Patient-Centered Value Assessment. Available at: <https://www.npcnow.org/guidingpractices>.

guidance that external organizations for organizations conducting evidence synthesis or technology assessment must meet.

Such standards should ensure methodological rigor and necessarily exclude organizations with a payor-focused mission or funding, as well as organizations that historically focus on CEA. This is important because of statutory prohibitions against CEA as well as the need to avoid analysis driven by a payor focus on cutting costs over patient needs by discounting clinical and non-clinical benefits that matter to patients, caregivers and society.

Adherence to appropriate standards for patient-centeredness and methodological rigor will result in avoidance of certain organizations that fail to meet those standards. In this regard, PhRMA urges CMS not to rely on evidence generated by the ICER or similar cost effectiveness analysis-driven organizations. ICER's grounding in threshold-based decision making, payor-centered mission, and methodological shortcomings make it and similar organizations ill-suited to the standards set in the IRA, as well as the goals of patient-centeredness and public trust. While many stakeholders have voiced particular concern over ICER's methods and governance, CMS should generally avoid relying on any technology assessment organizations that cannot demonstrate clear independence and patient-centeredness. This should also preclude reliance on other technology assessment organizations that primarily serve or are governed by payors, such as the Blue Cross Blue Shield Technology Evaluation Center or the Drug Effectiveness Review Project.

To date, ICER has fallen short of the types of standards that CMS should develop for setting the MFP. ICER's bias toward payor needs and cost-cutting has been seen in its drug-specific assessments, which often deviate from its own commitments to stakeholders to obtain predetermined, payor-driven objectives. Several months before ICER's assessment of remdesivir, a treatment for COVID-19, ICER committed to include the societal perspective as a co-base case alongside the health system perspective in its assessments, when disease areas met certain criteria.¹¹² However, in spite of its prior commitment – and COVID-19 clearly meeting the established criteria – ICER declined to develop a co-base case based on the societal perspective, resulting in a skewed assessment of remdesivir's value. This ignored important societal benefits of an effective treatment for COVID-19, such as reducing the risk associated with reopening business and schools. ICER was criticized for this decision, not only by the biopharmaceutical industry, but by former employees and academic thought-leaders.¹¹³

ICER's assessments have also fallen short of standards for patient-centeredness in evidence assessment. Although ICER includes outcomes that matter to patients and caregivers in the “other benefits and disadvantages” or “contextual consideration” portion of its report, it fails to include the outcomes in its recommendations on its health-benefit price benchmark of a drug. For example, in ICER's review of treatments for myasthenia gravis, ICER omitted multiple outcomes from its quantitative assessment of the treatment's value, including impact on caregivers, chronic fatigue, and impact on mental health, that were cited by patient and caregiver advocates as important.¹¹⁴

Importantly, ICER's assessments heavily rely on the QALY metric, which as discussed above has a history of devaluing the lives of vulnerable populations. While it is now recognized by many stakeholders and researchers that traditional methods of QALY-based value assessment are controversial and outmoded (and ICER itself has acknowledged these concerns¹¹⁵), ICER persists in generating health-benefit price benchmarks based on QALYs and similarly flawed metrics for every assessment it conducts. ICER's failure to acknowledge the concerns of

¹¹² Institute for Clinical and Economic Review. (2020). 2020 – 2023 Value Assessment Framework. Available at: https://icer.org/wp-content/uploads/2020/10/ICER_2020_2023_VAF_102220.pdf.

¹¹³ Cohen, J. T., Neumann, P. J., Ollendorf, D. A. (2020). Valuing And Pricing Remdesivir: Should Drug Makers Get Paid For Helping Us Get Back To Work? Health Affairs Forefront. Available at: <https://www.healthaffairs.org/doi/10.1377/forefront.20200518.966027/full/>.

¹¹⁴ ICER. (2021). Eculizumab and Efgartigimod for the Treatment of Myasthenia Gravis: Effectiveness and Value. Available at: https://icer.org/wp-content/uploads/2021/03/ICER_Myasthenia-Gravis_Final-Report_12-Month-Check-Up_12122.pdf.

¹¹⁵ ICER. (2018). The QALY: Rewarding the Care That Most Improves Patients' Lives. Available at: https://icer-review.org/wp-content/uploads/2018/12/QALY_evLYG_FINAL.pdf.

stakeholders with regard to the QALY and other issues is why CMS should avoid reliance on ICER and other similar organizations when determining MFPs.

j. Consideration of Real-World Evidence (Section 50.2)

We appreciate CMS' statement that it will consider RWE as part of its process for setting MFPs. PhRMA hopes that in determining MFPs for selected drugs, CMS will review and incorporate a broad range of rigorous scientific evidence, including data resulting from real-world experience with the drug's use, including the RWE that has become available in the years since a treatment's FDA approval.

However, we are concerned by 1) the lack of specifics in the Guidance as to the standards for quality CMS will use to determine whether individual pieces of RWE should be relied upon to determine MFPs, and 2) the lack of specifics as to how RWE will be weighed against other forms of evidence. These are important details that manufacturers, as well as other stakeholders, require in order to understand how CMS intends to arrive at MFPs for selected drugs.

RWE can come from a variety of sources, including electronic health records, payor administrative claims, implementation studies and patient registries and represents a valuable source of information about the real-world benefits and risks of a medicine. CMS should consider evidence from all these sources, and incorporate a broad range of rigorous scientific evidence, including data resulting from real-world experience with the drug's use, including the RWE that has become available in the years since a treatment's FDA approval.

Particularly for a drug that has been on the market seven or more years, RWE can provide valuable insights into how the drug works in a real-world clinical setting, including for different subpopulations and in different contexts. For example, an ongoing study of 133 people with HIV demonstrated the benefits of a long-acting antiretroviral treatment (LA-ART) to individuals with HIV. The study showed that the LA-ART given every four to eight weeks, and delivered with comprehensive support services, suppressed HIV in people who were previously not virologically suppressed. The study focused on reaching people who have historically had decreased access to antiretroviral therapy (ART), including people experiencing housing insecurity, mental illnesses, and substance use disorders, and who may have been included in clinical trials.¹¹⁶

However, use of RWE and the consideration and weight it is given varies amongst organizations and decision-makers. This makes it important for CMS to include more explicit discussion of its approach to considering RWE as part of its MFP methodology than what was included in the Guidance. ***PhRMA recommends that CMS appropriately consider rigorous RWE generated after initial FDA approval related to the benefits and impact of a selected drug.*** Consideration of RWE will be particularly important to ensure CMS can properly assess and value the full range of benefits and elements of unmet need discussed below, such as improved adherence, patient convenience, and broad health care cost offsets.

k. Consideration of Specific Patient Populations (Section 50.2)

CMS states that it will consider research on and RWE relating to Medicare populations – including individuals with disabilities, end-stage renal disease (ESRD) and aged populations – as particularly important. In addition, CMS will prioritize research specifically focused on these populations over studies that include outcomes for these populations, but in which these populations were not the primary focus. CMS states that it will consider the effects of the selected drug and its therapeutic alternative(s) on specific populations, including individuals with disabilities, the elderly, the terminally ill, and children.

¹¹⁶ Long-acting antiretroviral therapy suppresses HIV among people with unstable housing, mental illnesses, substance use disorders. (Feb 21, 2023). Available at: <https://www.nih.gov/news-events/news-releases/long-acting-antiretroviral-therapy-suppresses-hiv-among-people-unstable-housing-mental-illnesses-substance-use-disorders>.

Because patient sub-populations can differ in their response to or preference for a therapy, a variety of treatment options may be required to optimize treatment and provide the most clinical benefit to a patient. CMS recognition of patient heterogeneity is particularly important to ensure alignment with the emergence of personalized medicine. While the sub-populations listed above are important, PhRMA recommends CMS consider additional subgroups as well, including those based on factors such as genomics, preferences, co-morbidities, and marginalized populations experiencing avoidable disparities in health outcomes.

This consideration is critical because the value individual patients and patient subgroups place on benefits and impacts, or their unmet needs, can vary. Studies have long shown that not only do patients place significant emphasis on benefits other than prolonged survival or cost, but that these preferences vary considerably depending on factors such as type and severity of disease and individual life circumstances. For example, research has shown that when asked to weigh different treatment impacts (e.g., effect on disease progression, effect on relapse rate, effect on multiple sclerosis (MS) symptoms), preferences among patients with MS were highly diverse. In most categories, patient opinions were more varied than those of other stakeholders, including clinicians or payors.¹¹⁷ In order to capture this diversity, CMS needs to consider all relevant sub-populations for the selected drug.

III. Negotiation Process (Section 60)

Section 1194 of the SSA, requires a “consistent methodology and process” for setting MFPs, and that these prices be “fair.” CMS has a critical opportunity to design this consistent methodology to ensure fair prices that account for reduced access to medicines in Medicare and loss of future treatments and cures.

Unfortunately, CMS’ Guidance provides no assurance that the Agency will meet this standard. Rather than describing a “consistent methodology and process,” CMS proposes an unworkable and subjective framework for setting MFPs. Furthermore, the process for price setting signals that CMS intends to provide only the most limited opportunities for stakeholders, such as patients and clinicians, to have input into the Program.

While CMS recognizes the importance of ensuring the rigor of the research and evidence synthesis it relies on in MFP decision-making, the Guidance fails to describe a process or standards for ensuring that its MFP determinations are rooted in patient-centeredness and methodological rigor. To help address this, ***PhRMA strongly recommends that prior to making its initial offer to the manufacturer, CMS make available to the public key elements of its MFP analysis. and provide an opportunity for the public to comment on them. This should include, but not be limited to:***

- ***Therapeutic alternative(s) CMS has identified for any selected drug it is considering (for each indication);***
- ***Data and analysis CMS developed and considered supporting each factor, including evidence provided by third parties engaged formally or informally by CMS;***
- ***Benefits and impacts of a selected drug CMS intends to consider; and***
- ***Stakeholders, and other government agencies and organizations CMS intends to engage, formally or informally.***

Below we outline specific concerns with the proposals in the Guidance, as well as concrete recommendations for how CMS can address these concerns, mitigate harm to patients, and recognize innovation in implementing the Program.

¹¹⁷ Nash, B. Mowry, S. McQueen, R. B., Longman, R. (2017). People with MS value therapies differently than do physicians or payers. Available at: <https://realendpoints.com/wp-content/uploads/2017/12/PhRMA-white-paper-final.pdf>.

a. Price Setting Methodology

CMS proposes as potential starting points for the initial offer: 1) Part D net price or Part B average sales price (ASP) of the selected drug; 2) Part D net price(s) and/or Part B ASP of therapeutic alternative(s); or 3) FSS or “Big Four” Agencies price either for selected drugs with no therapeutic alternative(s) or for selected drugs that have therapeutic alternative(s) with net prices or ASPs greater than the statutory ceiling. This approach is misguided and will result in egregiously low prices previously criticized and rejected by stakeholders. Furthermore, the approach proposed by CMS is arguably in tension with the statute. While the statute requires CMS to achieve the lowest “fair” price “for each selected drug,”¹¹⁸ CMS’ approach looks primarily at therapeutic alternative(s) to the selected drug, rather than the selected drug itself.

The approach relies upon therapeutic reference pricing, which resembles the “least costly alternative (LCA)” policies previously attempted by CMS and struck down by a federal court more than a decade ago.¹¹⁹ This approach would give CMS broad authority to make judgments about clinical “similarity” for a broad range of medicines. It would also overlook significant differences in the needs of patients, many of whom do not fit value judgments based on broad, average results. Individual patient differences occur due to several factors, such as genetic variation, differences in clinical characteristics, co-morbidities, and quality-of-life preferences. For example, the five different larifuno-oncology agents recommended for treatment of metastatic non-small cell lung cancer (mNSCLC) can appear similar when looking at treatment effects based on averages,¹²⁰ however, different treatments are recommended based on patient subgroup¹²¹ – defined by PD-L1 expression – because overall survival can increase by as much as 164 percent¹²² based on the patient characteristics. Furthermore, patients can value quality-of-life factors differently with treatments that require less frequent visits to a provider or that can be delivered by mail often being of higher value to Hispanic and Black patients who are more likely to live in a neighborhood impacted by pharmacy deserts. As a result, imposing policies like LCA that rely on broad judgments of comparative effectiveness of treatments will overlook important differences in the way individual patients respond to treatment, and downstream, can create barriers to access to important treatments. When proposed in other contexts, patient advocates have reiterated these concerns, “We cannot achieve a healthier society simply by making investments based on what is the cheapest.”¹²³

Furthermore, PhRMA does not support CMS’ proposed reliance on the FSS price or the “Big Four” price. Domestic reference pricing at these prices has also been soundly rejected by policymakers, including very recently by Congress – during Senate floor consideration of the IRA, Senator Bernie Sanders offered an amendment to tie drug prices in Medicare to those used in the VA. This amendment failed overwhelmingly by a vote of 99 to one.¹²⁴

FSS contracts are not designed or intended to establish a pricing benchmark for medicines, and instead are procurement contracts that direct federal purchasers use to purchase items and services from vendors and suppliers. Specifically, FSS purchasers acquire medicines on the FSS directly from wholesalers or biopharmaceutical manufacturers at the contracted price and then furnish such medicines to certain patients within “closed” health care delivery systems. Further, FSS and “Big Four” prices do not reflect the full “cost” of the

¹¹⁸ 42 U.S.C. § 1320f-3(b)(1).

¹¹⁹ Available at https://ecf.dcd.uscourts.gov/cgi-bin/show_public_doc?2008cv1032-22.

¹²⁰ Cui P, Li R, Huang Z, Wu Z, Tao H, Zhang S, Hu Y. (2020). “Comparative effectiveness of pembrolizumab vs nivolumab in patients with recurrent or advanced NSCLC.” *Nature*. 10:13160. Available at: <https://doi.org/10.1038/s41598-020-70207-7>.

¹²¹ Bradley CA. (2019). “Pembrolizumab improves OS across PD-L1 subgroups.” *Nature Reviews*. 16; 403. Available at: <https://www.nature.com/articles/s41571-019-0213-5.pdf?origin=ppub>.

¹²² Mok TS, Wu Y, Jyda I, Kowalski DM, Cho BC, Turna HZ, et al. (2019). “Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled, phase 3 trial.” *The Lancet*. 393: 10183; 1819- 1830. Available at: [https://doi.org/10.1016/S0140-6736\(18\)32409-7](https://doi.org/10.1016/S0140-6736(18)32409-7).

¹²³ Thorpe, K. (2014). MedPAC recommendations miss the mark. *The Hill*. Available at: <https://thehill.com/blogs/congress-blog/healthcare/203976-medpac-recommendations-miss-the-mark/>.

¹²⁴ S. Amdt. 5210 to S. Amdt. 5194 to H.R 5376 https://www.senate.gov/legislative/LIS/roll_call_votes/vote1172/vote_117_2_00288.htm.

medicine. As noted in a recent report by the CBO, comparing prescription drug prices among government programs is difficult, and average prices are not directly comparable because the price of medicines in federal programs like Medicare, which uses a retail distribution network, must consider pharmacy storage and dispensing costs and profits. In contrast, average FSS and “Big Four” prices (which are two distinct prices authorized by law for different purchasers) do not consider wholesaler profits, storage, distribution, or pharmacy/physician dispensing.¹²⁵ They are, therefore, not reasonable starting points for CMS’ price setting process.

In addition, reliance on FSS and “Big Four” prices could result in manufacturers effectively being assessed an inflation rebate twice. Per statutory requirements of the Veterans Health Care Act, some medicines on the FSS have an additional inflationary rebate component factored into the Federal Ceiling Price, while medicines in Medicare will have a separate inflation rebate if pricing metrics increase faster than inflation.¹²⁶

Recommended Approaches to Determining MFPs for Selected Drugs

PhRMA believes that instead of haphazardly piecing together an approach to price setting based on previously rejected policy ideas, CMS should adopt a methodology in the initial years of the program that acknowledges both the exceptionally challenging task at hand, as well as the substantial potential harm to patients and innovation if CMS undervalues selected medicines. It is broadly understood that CMS is establishing a price setting program for the first time, without necessary experience in this area. There is also extraordinary burden on manufacturers to submit data and engage in this complicated process with little information or advance notice. Given this confluence of factors, ***PhRMA recommends that CMS ensure all MFPs are set at the statutory ceiling price beginning with IPAY 2026, and for several subsequent price applicability years.***

Beyond the first several years of the Program, CMS should consider the fundamental problems posed by the IRA’s price setting framework and work to adopt policies that mitigate those problems. One example is the reduced incentives for continued R&D for small molecule medicines created by the IRA’s criteria for selecting drugs, which could result in CMS selecting small molecule drugs a mere seven years after their initial FDA approval. The IRA effectively reduces the period of exclusivity from the current effective average of 13 to 14 years to nine years for small molecule drugs selected for price setting (and CMS’ decision to finalize a “qualifying single source drug” (QSSD) definition based on active moiety heightens this effect).¹²⁷ Nine years will simply not be enough time for many drugs in development to earn a return that warrants the large and uncertain investment a company must make to bring a drug to market. Recent empirical research shows that, on average, about half of a product’s revenues are earned during years 10 through 13 after approval, and very few drugs have earned a return justifying investment within nine years after approval.¹²⁸ And as previously noted, recoupment of investment itself isn’t sufficient—a “cost-plus” approach to setting MFPs will also undoubtedly devastate biopharmaceutical innovation.

For these reasons, ***PhRMA recommends setting the MFP for selected drugs that have been on the market for less than 13 years at or near the ceiling price set forth in statute.*** This would be in keeping with the overall intent of the IRA, which sets ceiling prices at different levels according to the time since FDA approval.

CMS should also recognize in setting MFPs that the stated intent of the price setting provisions was to address the lack of competition for older drugs from generics or biosimilars. This objective takes a narrow view of

¹²⁵ CBO. (2021). A Comparison of Brand-Name Drug Prices Among Selected Federal Programs.

Available at: <https://www.cbo.gov/publication/57007>. CBO notes that FSS and “Big Four” prices are not retail prices. Specifically, “Pharmacy dispensing fees are incorporated into the prices in Medicare Part D, Medicaid, and the TRICARE retail pharmacy network. However, the prices for VA and DoD...do not include the agencies’ costs of dispensing drugs.”

¹²⁶ See SSA §§ 1847A(i) and 1860D-14B.

¹²⁷ Grabowski H, Long G, Mortimer R, Bilginsoy M. (2021). Continuing trends in U.S. brand-name and generic drug competition. J Med Econ.;24(1):908-917. DOI: 10.1080/13696998.2021.1952795. PMID: 34253119.

¹²⁸ Tewari, A. et al. (2022) The Drug Pricing Handbook - Everything you Need to Know. Jefferies Research. September 15, 2022. p.4.

competition: for some products, brand-to-brand competition occurs prior to generic or biosimilar entry, which has resulted in payors negotiating steep rebates and a net price that falls below the statutorily mandated discount. CMS has an opportunity to acknowledge this competition by setting MFPs for such drugs at the ceiling price.

The statutory ceiling price for selected drugs is the lower of two options – either the net price (or ASP) of a selected drug, or a significant percentage off of the selected drug’s non-FAMP. ***PhRMA recommends that if a selected drug’s statutory ceiling price is the net price, then the MFP should be set at the ceiling price (the net price) for the selected drug.*** This would acknowledge drugs for which brand-to-brand competition has resulted in meaningful savings, and therefore, were not the target of the policy. Furthermore, it is operationally feasible for CMS, as CMS has access to the necessary price data and must calculate a net price to determine the ceiling price.

There are two other instances in which PhRMA specifically recommends CMS set the MFPs at the ceiling price beyond the first several years of the Program: drugs that represent a substantial unmet need and drugs that represent a significant therapeutic advance against therapeutic alternative(s). Identifying these types of discrete factors or circumstances that will result in MFPs at or close to the ceiling price would provide at least some predictability in CMS’ decision-making process. Those recommendations are discussed below in subsections (f) (Unmet Medical Need) and (g) (Therapeutic Advance).

b. Weighting of Factors

As noted by CMS in the Guidance, the statute establishes two sets of factors that CMS must consider when determining the offers and counteroffers to reach a drug’s MFP: “manufacturer-specific data” and evidence regarding alternative treatments. As CMS has acknowledged, the statute does not specify “how CMS should determine an initial offer nor how or to what degree each factor should be considered.”¹²⁹ PhRMA is concerned by CMS’ failure to clarify how it will use its discretion in considering and weighting the factors. ***PhRMA strongly recommends that CMS generally place greater emphasis on the factors related to the benefits medicines offer to patients included in section 1194(e)(2).*** These benefits include not just the benefit to patients, but also to caregivers and society. An emphasis on these benefits and factors may somewhat mitigate against the disincentives inherent in government price setting for continued innovation resulting from price setting by reducing the penalty on drugs with significant demonstrated benefits that accumulate over the course of a product’s life cycle. We note, however, that the mitigation is limited by the fact that the statutory ceiling price applies even when a higher price would be set based on the factors related to the therapeutic benefits medicines offer to patients.

As a corollary, CMS should place less weight on factors that would diminish drugs’ benefits and could stagnate innovation if overweighted. This includes most of the factors listed in section 1194(e)(1), such as cost of production, costs of R&D, and federal funding toward the development of a selected drug. If CMS places too much importance on these factors, the result could be a “cost recovery” pricing model for selected drugs, in which the price is set to allow the manufacturer to recoup only the cost of producing the drug, including the cost of R&D. Basing prices for drugs on costs incurred by the manufacturer, instead of the value and benefits conferred by the innovation, sends perverse, unintended signals to manufacturers that devalue and disincentivize R&D and pose a significant threat to innovation and progress for future medicines. Placing greater weight on the factors in section 1194(e)(2) will help incentivize continued medicine advances and innovation. In addition, to avoid a chilling effect on post-approval research, factors used to determine the MFP should include consideration of both existing and pending patent protections, existing regulatory data exclusivities, and labeled as well as pending indications in addition to other factors, such as ongoing clinical development programs.

¹²⁹ Guidance, section 60.3.

c. Therapeutic Alternative(s)

For IPAY 2026, CMS will identify the selected drug's FDA-approved indications that are neither excluded from coverage nor otherwise restricted. CMS will then identify pharmaceutical therapeutic alternative(s) for each indication of the selected drug, using data submitted by the Primary Manufacturer and the public, along with widely accepted clinical guidelines and peer-reviewed studies. CMS also will consider clinical evidence via literature searches.

Although PhRMA strongly disagrees with CMS' proposal to use therapeutic reference pricing as the starting point for MFP determinations, PhRMA agrees that therapeutic alternative(s) should generally be limited to pharmaceutical therapeutic alternative(s). We believe that some of the resources CMS cites in the Guidance, such as clinical guidelines, will be very helpful in identifying therapeutic alternative(s) for certain classes of drugs.

However, ***PhRMA believes that experts, including manufacturers and clinicians, should be the primary resources for determining therapeutic alternative(s), and CMS should go beyond what the Agency laid out in the Guidance to engage key stakeholders in the selection of therapeutic alternative(s).*** PhRMA notes that manufacturers are in a strong and unique position to inform CMS' determination of appropriate therapeutic alternative(s) for a selected drug, based on their extensive expertise and research on the benefits and impacts of their medicines throughout the product lifecycle. Manufacturer-sponsored research frequently includes comparative effectiveness research, which requires selection of a clinically appropriate comparator. Additionally, clinicians with disease-specific expertise and disease-specific clinical guidelines generated by clinicians should also play a meaningful role in CMS' determination of a selected drug's therapeutic alternative(s). Simply asking stakeholders to provide information through an ICR is an insufficient means of engaging stakeholders on this key issue. Clinician and patient engagement will be discussed in further detail in section III.t. of this letter.

Procedurally, it is unclear when CMS will identify the therapeutic alternative(s) for a selected drug and communicate that information to the manufacturer. PhRMA notes that if CMS fails to communicate the therapeutic alternative(s) for the selected drug early enough in the process, the manufacturer and stakeholders will be unable to include the required information in their data submissions to the Agency. ***PhRMA strongly recommends that CMS publicly identify the therapeutic alternative(s) selected, including if based on information and feedback received through the ICR, and allow the manufacturer and stakeholders to provide feedback on CMS' proposal.***

When determining the therapeutic alternative for a selected drug, ***PhRMA recommends that CMS use "clinical appropriateness" as the standard for decision-making.*** In order to determine the clinical appropriateness of a therapeutic alternative, CMS should do the following:

- Engage meaningfully with the manufacturer on potential therapeutic alternative(s) and comparator(s);
- Look to clinician guidance, including physician-driven evidence-based clinical guidelines, as a resource; and
- Reference other widely recognized, scientifically rigorous, evidence-driven resources to identify therapeutic alternative(s).

Selection of the appropriate therapeutic alternative(s) in assessments of the comparative effectiveness of treatments is complex and can involve subjective judgments. Both the significant complexity of this issue, as well as the consequences of CMS choosing an inappropriate therapeutic alternative for its decision-making, is illustrated in price setting systems outside the U.S. Germany provides perhaps the starkest case study for the magnitude of the impact that inappropriate comparator selection can have in a large market. Problems with comparator selection, combined with rigidity in accepting indirect comparisons, is one of the main failings of the German system. In Germany, 70 percent of assessments by the German Federal Joint Committee (G-BA) are

negative for non-orphan innovative medicines, and most rejections (72 percent) are for not presenting data against the G-BA chosen comparator.¹³⁰ Yet, research shows that in 43 percent of cases, medical societies opposed the comparator selected by the G-BA.¹³¹

Beyond ensuring that the chosen therapeutic alternative is clinically appropriate, ***PhRMA strongly cautions that cost cannot play a role in determination of a selected drug's therapeutic alternative or clinical comparator.***¹³²

Experience in other countries illustrates how cost factors have the potential to skew choice of comparators to achieve a desired cost-containment outcome. The Agency should establish standards and procedures for comparator selection that protect against this. In Germany, for example, because the price of a drug is based on its comparative clinical effectiveness relative to a comparator, Germany's choice for a comparator has a considerable impact on the reimbursement price.¹³³ Germany uses the least costly available comparator as the price benchmark when the G-BA determines there is no benefit, even if the treatments have differences that are significant from a patient or caregiver perspective, such as reduced side effects or mode of administration.¹³⁴ PhRMA strongly cautions against adopting this approach.

d. Benefits and Impacts

In assessing comparative effectiveness between a selected drug and therapeutic alternative(s), CMS plans to identify outcomes to evaluate for each of the selected drug's indications and consider the safety profiles. When evaluating clinical benefits of the selected drug and its therapeutic alternative(s), CMS intends to consider health outcomes, intermediate outcomes, surrogate endpoints, patient-reported outcomes, and patient experience.

PhRMA is deeply concerned with CMS' description of the outcomes that it will consider in determining how a selected drug compares to a therapeutic alternative, particularly the narrow and vague description of the outcomes that CMS will consider, as well as its failure to center the decision-making on patients. In order to preserve patient access and biopharmaceutical innovation, ***PhRMA recommends that CMS consider the broad range of benefits and impacts of a selected drug, with particular focus on those that are important to patients, caregivers, and society.*** CMS' statement that it intends to consider health outcomes such as changes in symptoms or other factors that are of importance to a person and patient-reported outcomes is insufficient reassurance that patients will play a meaningful role in determining what benefits and impacts are prioritized as part of CMS' decision-making process. As noted by the Patient-Centered Outcomes Research Institute (PCORI) in its 2022 review of 200 publications from a range of different health organizations related to the discussion of value, "When it comes to defining patient-centered value, most stakeholders agree that it includes health and non-health outcomes and monetary and non-monetary impacts that are defined based on patient goals, expectations, and experiences."¹³⁵

It is widely recognized that patients value a range of benefits of medicines beyond clinical endpoints evaluated in research.¹³⁶ For example, benefits that may be valued by patients, but typically are not captured in research, include the range of potential side effects, impact on patients' ability to carry out basic functions, and quality of

¹³⁰ AMNOG Monitor. Early benefit assessment: detailed analysis of all G-BA resolutions. Available at: <https://www.amnog-monitor.com/>.

¹³¹ Bleß et al., (2016). Impact of scientific opinions in the benefit assessment of medicinal products. IGES Institute.

¹³² While we recognize the statute mentions the "costs of...existing therapeutic alternatives," CMS should only use this in determining a selected drug's MFP, not in its initial determination of a drug's therapeutic alternative(s).

¹³³ Sieler, S. R., T., Brinkmann-Sass, C., Sear, R. (2015). AMNOG Revisited. McKinsey & Company. Available at: <https://www.mckinsey.com/industries/life-sciences/our-insights/amnog-revisited>.

¹³⁴ Ivandik, V. (2014). Requirements for benefit assessment in Germany and England-overview and comparison." Health Economics Review. Available at: <http://www.healtheconomicsreview.com/content/4/1/12>.

¹³⁵ Havjou, O., Bradley C., D'Angelo, S., Giombi, K., Honeycutt, A. (2022). Landscape Review and Summary of Patient and Stakeholder Perspectives on Value in Health and Health Care. PCORI. Available at: <https://www.pcori.org/sites/default/files/PCORI-Landscape-Review-Summary-Patient-Stakeholder-Perspectives-Value-Health-Health-Care-August-2022.pdf>.

¹³⁶ Neumann, P. J., Garrison, L. P., Willke, R. J. (2022). The history and future of the "ISPOR value flower": Addressing limitations of conventional cost-effectiveness analysis. Value in Health, 25(4), 558–565. Available at: <https://doi.org/10.1016/j.jval.2022.01.010>.

life. Other non-clinical-related benefits also can be very important, such as the utility of reduced frequency of dosing through a long-acting formulation and reduced caregiver burden. CMS should ensure that its evaluations of therapeutic advances capture the value of and give significant weight to these benefits and impacts in selected drugs' MFPs to maintain incentives for manufacturers to continue meeting these needs.

In addition to capturing this full range of outcomes, CMS' methodology should ensure that when patient, caregiver, or clinician perspectives differ from those of payors, the former are prioritized. A survey focused on MS that included patients, neurologists who treat MS, and payors found significant variability in the value of different impacts among the different stakeholder groups. For example, MS patients placed the most value on treatment of mobility and upper limb function, whereas neurologists placed the least value on this combination of symptoms.¹³⁷ CMS must not evaluate therapeutic advances in a vacuum.

As noted above, ***PhRMA believes that benefits and impacts of a selected drug compared to its therapeutic alternative(s) must incorporate consideration of a drug's impact on society, including benefits to patient caregivers and their families.*** CMS does not mention society or caregivers at all in the discussion of outcomes in the Guidance even though approximately one out of every five Americans is a caregiver.¹³⁸ Failing to account for the benefits and impacts of a medicine to society could inappropriately reduce CMS' determination of a selected drug's MFP. For example, a recent study found that inclusion of caregiver impacts can have a significant effect on an assessment of an intervention's value.¹³⁹ Important disease-related societal impacts, such as a reduction in costs associated with incarceration rates (such as with treatments for alcohol use or mental illness), environmental impacts, and the cost of social services, should also be included in the MFP determination.

When a drug provides a significant benefit to society, CMS should consider increasing the MFP accordingly, including setting the price at or near the statutory ceiling. This should include any selected drug that is a vaccine, due to the unique circumstances of vaccines and substantial patient and public health benefits that they confer. Vaccines represent some of the most impactful advances in public health, helping to prevent the spread of many infectious diseases and, in many parts of the world, eliminating some of the most devastating conditions. There is no better case study for the importance of vaccines than the biopharmaceutical industry's response to the recent COVID-19 pandemic. The importance of vaccination goes beyond global pandemics, however – in the U.S. today, 16 diseases are now preventable as a result of childhood vaccines,¹⁴⁰ and routine immunization of U.S. children born between 1994 and 2018 has prevented more than 419 million illnesses.¹⁴¹ The IRA itself recognizes the unique importance of vaccines, eliminating patient cost sharing for adult vaccines under Medicare Part D. CMS should recognize this in setting final MFPs as well by accounting for vaccines' remarkable benefits to public health.

PhRMA also has concerns about CMS' approach to identifying benefits and impacts; CMS should meaningfully engage with manufacturers and patients to identify the relevant benefits and impacts, rather than predominantly relying on literature reviews or ICRs. Specific recommendations for how CMS should engage with patients and physicians are discussed in section III.t. of this comment letter.

¹³⁷ Nash, B., Mowry, S., McQueen, R. B. (2017). People with MS value therapies differently than do physicians or payers. RealEndpoints. Available at: <https://realendpoints.com/wp-content/uploads/2017/12/PhRMA-white-paper-final.pdf>.

¹³⁸ National Alliance for Caregiving and AARP. (2020). Caregiving in the U.S. 2020. NAC. Available at: <https://www.caregiving.org/research/caregiving-in-the-us/>.

¹³⁹ Lin PJ, D'Cruz B, Leech AA, Neumann PJ, Sanon Aigbogun M, Oberdhan D, Lavelle TA. (2019). Family and Caregiver Spillover Effects in Cost-Utility Analyses of Alzheimer's Disease Interventions. *Pharmacoeconomics*;37(4):597-608. DOI: 10.1007/s40273-019-00788-3. PMID: 30903567.

¹⁴⁰ Centers for Disease Control and Prevention (CDC). (2019), Diseases & the Vaccines that Prevent Them. CDC. Available at: <https://www.cdc.gov/vaccines/parents/diseases/index.html>.

¹⁴¹ CDC. (2022). VFC Infographic: Protecting America's Children Every Day. Updated 2021 analysis using methods from "Benefits from Immunization during the Vaccines for Children Program Era – United States, 1994 – 2021. *MMWR*. 25 April 2014. Available at: <https://www.cdc.gov/vaccines/programs/vfc/protecting-children.html>.

PhRMA notes that accounting for a broad range of benefits and impacts aligns with input from experts in the fields of comparative effectiveness research and HTA.¹⁴² Best practices for HTA include capturing a range of potential “value elements,” including treatment adherence, fear of contagion, the value of hope, and scientific spillover effects.¹⁴³ Although they may be difficult to quantify, individuals and organizations, such as the Innovation and Value Initiative,¹⁴⁴ are developing methods to incorporate some of these value elements, such as insurance value and real option value into research. CMS can contribute to progress in this field by identifying these outcomes as important in its MFP-setting deliberations.

Input from clinicians, patients and caregivers with disease-specific experience will be particularly important in order to accurately identify the benefits and impacts of a treatment that matters to patients, caregivers, and society. As such, CMS will need to establish a process to engage with stakeholders, beyond soliciting feedback through an ICR. ***PhRMA recommends that following the ICR and prior to CMS’ initial offer, CMS engage the manufacturer and other stakeholders in direct conversations, in which the Agency shares the benefits and impacts it identified as meaningful through the ICR, as well as its own research, and allows the manufacturer and stakeholders to provide feedback on the Agency’s findings.***

Second, CMS should be transparent with both manufacturers and stakeholders as to the benefits and impacts that CMS considered, and how the benefits and impacts influenced the MFP. PhRMA recommends CMS provide this detail in both the justification for CMS’ initial MFP offer (section 1194(b)(2)(B)), as well as the explanation for a drug’s MFP (1195(a)(2)). Specifically, ***PhRMA recommends that CMS include in its explanation of a selected drug’s MFP a table listing the following elements:***

- ***The benefits and impacts across all indications, clinical and non-clinical, that CMS considered in its determination of a selected drug’s MFP;***
- ***CMS’ process for determining benefits and impacts to include in its determination of the MFP, including a list of each stakeholder consulted;***
- ***Information about the relative weight given to each benefit and impact considered during the determination of the MFP;***
- ***Source(s) of evidence for each benefit and impact; and***
- ***How each benefit and impact influenced the final MFP.***

CMS’ assessment of how a drug performs on these benefits and impacts (derived from stakeholder feedback) should form the foundation of how it arrives at a selected drug’s MFP. Furthermore, this level of transparency – balanced with important data protections – is imperative so that manufacturers and stakeholders can have confidence in CMS’ conclusions, and so that manufacturers can plan for evidence generation in anticipation of their drug’s selection for the Program.

e. Cost of Selected Drug and Therapeutic Alternative(s)

As previously stated, PhRMA has significant concerns with CMS’ proposal to use therapeutic reference pricing as the foundation of its approach to setting prices for selected drugs. However, we recognize that the statute includes as a factor “the extent to which such [MFP] drug represents a therapeutic advance as compared to

¹⁴² Neumann, P. J., Willke, R. J., Garrison, L. P. (2018). A Health Economics Approach to US Value Assessment Frameworks—Summary and Recommendations of the ISPOR Special Task Force Report. *Value in Health*, 21(2), 119–123. Available at: <https://doi.org/10.1016/j.jval.2017.12.012>.

¹⁴³ Neumann PJ, Garrison LP, Willke RJ. (2022). The History and Future of the "ISPOR Value Flower": Addressing Limitations of Conventional Cost-Effectiveness Analysis. *Value Health*; 25(4):558-565. DOI: 10.1016/j.jval.2022.01.010. Epub 2022 Mar 9. PMID: 35279370.

¹⁴⁴ The Innovation and Value Initiative. <https://thevalueinitiative.org/>.

existing therapeutic alternatives and the costs of such existing therapeutic alternatives,” to the extent such information is available.

Should such information be available, PhRMA recommends that CMS interpret such language broadly, to include a consideration of a range of direct and indirect costs (such as the costs to caregivers, transportation costs, lost work time¹⁴⁵), and cost savings associated with appropriate use of a selected drug. Medicines not only improve and save lives, but also frequently help avoid other, often costly, health care services, such as emergency room visits, hospital stays, surgeries, and long-term care.¹⁴⁶ Health cost savings due to improved use of medicines are well-documented in public programs, including Medicare. For example, as a result of seniors and people with disabilities gaining Medicare Part D prescription drug coverage, Medicare saved \$27 billion due to improved adherence to congestive heart failure medications from 2010 to 2016.¹⁴⁷ Other federal agencies recognize these savings; the CBO explicitly accounts for Medicare savings from policies that increase the use of medicines due to reduced spending on other Medicare services.¹⁴⁸ By recognizing these savings in determining a selected drug’s MFP, CMS can provide an important signal to innovators that it recognizes the importance of medicines’ ability to save money for the health care system.

Additionally, PhRMA recommends that any data CMS relies upon to understand the cost of a drug reflect true net cost after rebates to Medicare. Manufacturers often pay substantial rebates to Medicare Part D plan sponsors and pharmacy benefit managers, but these price concessions are not reflected in Part D negotiated prices. According to government data, rebates can reduce average net costs for Part D plan sponsors by 40 percent or more for commonly used classes of medicines.¹⁴⁹ Government data also show that manufacturer rebates lowered total gross Part D expenditures by 22 percent in 2020¹⁵⁰ and that total Part D rebates paid by manufacturers increased by more than 400 percent between 2010 and 2020.¹⁵¹ These findings underscore the importance of CMS ensuring the data it uses to set the MFPs for selected drugs account for manufacturer rebates. PhRMA understands that CMS plans to identify the price¹⁵² of each therapeutic alternative covered by Part D, net of all price concessions, when developing a starting point for its initial MFP offer.

CMS should also account for the significant discounts on medicines provided under the 340B Drug Pricing Program. Ignoring these statutory discounts could lead to CMS setting an MFP that negatively impacts incentives for innovation. While the IRA forbids a duplicate 340B and MFP discount on a selected drug, without needed data for verification, manufacturers could be forced to pay steep discounts under both programs in addition to any commercial rebates owed to Part D plans and PBMs. Overall, 340B purchases are 17 percent of outpatient

¹⁴⁵ As of 2018, more than one in six Medicare beneficiaries – or 10.1 million people – were employed according to: Feder, J. M., Radley, D. C. (2020). COVID-19’s Impact on Older Workers: Employment, Income, and Medicare Spending. The Commonwealth Fund. Available at: https://www.commonwealthfund.org/sites/default/files/2020-10/Jacobson_COVID_impact_older_workers_ib_v3.pdf.

¹⁴⁶ PhRMA. (2022). 2022 Industry Profile Toolkit: Better Use of Medicines Can Improve Health Outcomes and Reduce the Use of Costly Medical Care. Available at: <https://phrma.org/resource-center/Topics/Research-and-Development/IndustryProfile-2022/2022-Industry-Profile-Toolkit-Better-Use-of-Medicines-Can-Improve-Health-Outcomes-and-Reduce-the-Use-of-Costly-Medical-Care>.

¹⁴⁷ CMS Press Release. (2017). Nearly 12 million people with Medicare have saved over \$26 billion on prescription drugs since 2010. Available at: <https://www.cms.gov/newsroom/press-releases/nearly-12-million-people-medicare-have-saved-over-26-billion-prescription-drugs-2010>.

¹⁴⁸ CBO. (November 2012). Offsetting Effects of Prescription Drug Use on Medicare’s Spending for Medical Services. Available at: <https://www.cbo.gov/sites/default/files/cbofiles/attachments/43741-MedicalOffsets-11-29-12.pdf>.

¹⁴⁹ Medicare Payment Advisory Commission. (July 2022) A Data Book: Health Care Spending and the Medicare Program. Available at: https://www.medpac.gov/wp-content/uploads/2022/07/July2022_MedPAC_DataBook_SEC_v2.pdf.

¹⁵⁰ Ibid.

¹⁵¹ Medicare Payment Advisory Commission. (2022). Initial findings from MedPAC’s analysis of Part D data on drug rebates and discounts. Available at: <https://www.medpac.gov/wp-content/uploads/2021/10/MedPAC-DIR-data-slides-April-2022.pdf>.

¹⁵² However, release of these data has significant competitive implications well beyond the Medicare program. Thus, specific pricing information by competitive products should never be shared.

branded drug sales.¹⁵³ Thus, if CMS were to ignore 340B discounts it would be missing a key factor that economists have stated can impact drug pricing.¹⁵⁴

f. Unmet Medical Need

PhRMA has significant concerns with CMS' unnecessarily narrow definition of "unmet medical need." CMS states that it will consider a selected drug as filling an unmet medical need if it treats a disease or condition where there are very limited or no other treatment options. In defining unmet medical need narrowly, CMS will exacerbate the harm to innovation that will result from Medicare price setting. If CMS fails to fully acknowledge innovation that addresses unmet patient needs, it will send signals that disincentivize ongoing innovation in areas where patients desperately need options.

CMS' definition is far narrower than the definition relied upon by the FDA, which facilitates several expedited programs (e.g., accelerated approval, breakthrough designation). In order to determine if a product meets the threshold for these programs, FDA defines unmet medical need as "a condition whose treatment or diagnosis is not addressed adequately by available therapy" that includes either "an immediate need for a defined population" or "a longer-term need for society."¹⁵⁵ FDA further clarifies that such a drug will treat a condition:

- Where there is no available therapy;
- Where there is available therapy, but the drug presents additional benefits; and
- Where the only available therapy was approved under the accelerated approval program and clinical benefit against the primary endpoint has not yet been verified.

Research has shown that the FDA definition of unmet need has significantly benefited patients by allowing the FDA to prioritize drugs that offer the largest health gains.¹⁵⁶ Therefore, given the significant risks to patients from CMS' inexplicably narrow definition, ***PhRMA recommends that at a minimum, CMS set the MFP for any selected drug that meets the FDA's definition of unmet need at the ceiling price, including those that met that definition at the time of approval.***

Furthermore, CMS should recognize other types of unmet need, including, but not limited to:

- Personalized medicines for certain subpopulations;
- Progress against rare and hard-to-treat illnesses;
- Treatments that improve patient adherence and quality of life;
- Need for additional treatments in a therapeutic area, such as a curative treatment;
- Treatments that improve the health of underserved and vulnerable communities who face health disparities;
- Treatments that benefit multiple common comorbidities at once; and

¹⁵³ BRG. (2020). Measuring the Relative Size of the 340B Program: 2020 Update. Available at: <https://media.thinkbrg.com/wp-content/uploads/2022/06/30124832/BRG-340B-Measuring-Relative-Size-2022.pdf>

¹⁵⁴ Conti RM, Bach PB. (2013). Cost consequences of the 340B drug discount program. JAMA. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4036617/>.

¹⁵⁵ FDA. (2014). Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. Available at: <https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf>.

¹⁵⁶ Chambers, J.D., Thorat, T., Wilkinson, C. L., Neumann, P. J. (2017). Drugs Cleared Through The FDA's Expedited Review Offer Greater Gains Than Drugs Approved By Conventional Process. Health Affairs;36(8):1408-1415. DOI: 10.1377/hlthaff.2016.1541.

- The stepwise nature of progress in which significant gains for patients are achieved via advances that build on one another.

Additionally, *PhRMA recommends that CMS consider unmet need across the product lifecycle*. The drugs selected by CMS will not be new to the market – although they may have met an unmet need at some point in their lifecycle, it is possible and even likely that treatment options will have changed by the time they are selected for the Program. This includes selected drugs that received expedited review by the FDA, which as noted above has an established definition of unmet need. Moreover, CMS’ consideration of whether a drug meets an unmet need after its initial FDA approval is important to preserve incentives for post-approval research, as previously discussed.

g. Therapeutic Advance

Section 1194(e)(2)(A) requires CMS to consider “[t]he extent to which such drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives.” Similar to our above comments on unmet need, it is critical that CMS acknowledge, in setting MFPs, medicines that represent an advance over existing treatments to maintain incentives for ongoing biopharmaceutical innovation. For drugs that represent a significant therapeutic advance, CMS should strongly consider setting MFPs at the statutory ceiling price.

Fortunately, CMS has both references within existing reimbursement policy, as well as resources, that can assist in defining and assessing selected drugs against this criterion. Furthermore, relying on existing Medicare policy would grant manufacturers of selected drugs critical predictability in understanding the criteria they must meet in order to obtain the statutory ceiling price for selected drugs.

One of these references is the New Technology Add-On Payment (NTAP) designation, which exists to ensure adequate reimbursement for certain new products that demonstrate, among other things, enhanced clinical improvement over existing technologies. In order to receive an NTAP, a product must demonstrate a substantial clinical improvement over existing services or technologies (in addition to two other distinct criteria), which is defined as “an advance that substantially improves, relative to...technologies previously available, the diagnosis or treatment of Medicare beneficiaries.” A product meets the substantial clinical improvement criterion for an NTAP if it satisfies one of the following factors:

- “The new...technology offers a treatment option for a patient population unresponsive to, or ineligible for, currently available treatments.
- The new...technology offers the ability to diagnose a medical condition in a patient population where that medical condition is currently undetectable or offers the ability to diagnose a medical condition earlier in a patient population than allowed by currently available methods and there must also be evidence that the use of the new...technology to make a diagnosis affects the management of the patient.
- The use of the new...technology significantly improves clinical outcomes relative to services or technologies previously available...
- The totality of the information otherwise demonstrates that the new...technology substantially improves, relative to technologies previously available, the diagnosis or treatment of Medicare beneficiaries.”¹⁵⁷

¹⁵⁷ 42 CFR § 412.87(b)(1)(ii) “Additional payment for new medical services and technologies: General provisions.”

The NTAP definition for substantial clinical improvement represents an established measurement that has been used for evaluating the value of certain products. By relying on an existing definition already in use in the Medicare program, CMS would be able to build on internal processes, experience and expertise used by the Agency to assess products that have applied for an NTAP. ***PhRMA recommends that CMS deem any drug that meets or has met the NTAP definition of “substantial clinical improvement” as representing a significant therapeutic advance and set the MFP at the ceiling price.*** This would not only apply to drugs that received official NTAP status previously, but any drug that currently meets the definition of “substantial clinical improvement” should be deemed as representing a therapeutic advance and should receive the ceiling price.

Additionally, PhRMA believes that highly credible, physician-driven oncology compendia, which CMS already relies on in other contexts, are important reference points for determining whether a treatment represents a therapeutic advance. Since 2008, the National Comprehensive Cancer Network (NCCN)’s Drug and Biologics Compendium has been one of these trusted resources. The NCCN Compendium’s aim is to provide stakeholders, including policymakers with information to “improve the effectiveness and quality of care for patients by developing and disseminating up-to-date, authoritative information.”¹⁵⁸ The recommendations in the Compendium are driven by stakeholders who should be central to the process for determining MFPs – multidisciplinary expert panels representing different specialties, including clinicians and patient advocates. Importantly, the Compendium is also updated on a regular basis to reflect currently available evidence.

Within the NCCN Compendium, indicated uses are categorized in a systematic approach that describes the type of evidence available for and the degree of consensus underlying each recommendation. NCCN considers evidence of both efficacy, safety of interventions, as well as an intervention’s toxicity. The two highest potential recommendation categories (of four) and their definitions are:

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate; and
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.¹⁵⁹

These two levels of recommendations reflect that a treatment is supported by strong evidence, as well as near uniform consensus (a majority vote of at least 85 percent of the expert panel) among experts that the intervention is appropriate for the listed indication. Given the consensus this designation reflects, and its credibility, ***PhRMA recommends that CMS deem any oncology drug receiving a Category 1 or 2A rating as a significant therapeutic advance and set MFPs for drugs that receive these designations in the Compendium at the ceiling price.***

h. Manufacturer Engagement

In the Guidance, CMS states that if the Primary Manufacturer does not accept CMS’ written initial offer and proposes a written counteroffer, which is subsequently not accepted by CMS, the Agency will invite the Primary Manufacturer to an in-person or virtual meeting that would take place within 30 days of CMS’ receipt of the Primary Manufacturer’s written counteroffer. After this initial meeting, each party would have the opportunity to request one additional meeting, for a maximum of three meetings between CMS and the Primary Manufacturer. In addition, all meetings must occur during a narrow time period – approximately four months’ time between the Primary Manufacturer’s written counteroffer to CMS and the end of the price setting period.

¹⁵⁸ National Comprehensive Cancer Network. (2008). “Submission Request to CMS.” Available at: <https://www.cms.gov/Medicare/Coverage/CoverageGenInfo/downloads/covdoc14.pdf>.

¹⁵⁹ National Comprehensive Cancer Network. “Definitions for NCCN Categories.” Available at: <https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines>.

While PhRMA appreciates CMS' willingness to provide some opportunities for manufacturer engagement, we believe that, in addition to the described meetings during the offer and counteroffer process, manufacturers should be permitted to engage with CMS much earlier in the process and should not have to wait until after an offer and counteroffer are rejected to meet with the Agency. PhRMA believes that CMS should meet with manufacturers at key decision points in the MFP process, similar to the opportunities for engagement that FDA provides manufacturers during the drug review and approval process. The purpose of the meetings would include providing an opportunity for a dialogue where CMS and manufacturers could ask questions of one another, including questions about the data CMS evaluates to determine a selected drug's MFP and allowing manufacturers to provide context and correct errors regarding the data that CMS relies on to set the MFP, including data given to CMS by third parties.

Specifically, *PhRMA recommends that CMS offer manufacturers the opportunity to meet¹⁶⁰ with relevant Agency staff at least three times prior to a counteroffer, including:*

- After drug selection but prior to initiation of the price setting process, to permit the manufacturer to provide critical input on issues such as potential evidence sources and comparator choice;
- Prior to CMS presenting the initial offer, so that CMS can provide information on its decision-making, analysis it conducted, and evidence sources, and permit the manufacturers to correct errors and provide important context; and
- After CMS presents the initial offer, so that manufacturers have the ability to discuss the data and assumptions that informed the initial offer.

The process that CMS proposes – whereby manufacturers would meet with CMS only after an initial offer and counteroffer are rejected, with all meetings forced into a four-month period – is insufficient and does not provide an opportunity for meaningful dialogue. While PhRMA reiterates that the Program cannot be thought of as a true negotiation, if CMS genuinely wants both a dialogue with manufacturers and a scientifically robust analysis of the clinical benefits of the selected drug, it should establish a process with sufficient time to meet and exchange information.

i. Patient and Clinician Engagement

CMS fails to outline a clear and meaningful process to engage with key stakeholders. Throughout the 91-page Guidance, there is barely any mention of the role of clinicians and patients as critically important stakeholders. The only formal opportunity for outside parties' input is through a generic ICR with a very short (30-day) deadline for input that begins after the list of selected drugs is published. PhRMA believes that providing clinicians and patients with only this limited role is a damaging misstep and lost opportunity that will significantly undermine the strength and reliability of the Program.

PhRMA strongly recommends that CMS develop a comprehensive and deliberative process to solicit input and advice from stakeholders, particularly patients, clinicians, and caregivers, at the start of the price setting process so they may provide relevant information to CMS in a timely manner. Patients¹⁶¹ and clinicians bring unique and essential expertise and perspectives on the value of medicines. Their firsthand experience with selected drugs in a real-world setting will likely lead them to develop perspectives that differ significantly from the perspectives of

¹⁶⁰ The definition of a "meeting" should be established by CMS. The FDA meeting criteria and tiering approach might be applicable for CMS. Please See: US Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products: Guidance for Industry. (DRAFT GUIDANCE). December 2017, Procedural.

¹⁶¹ CMS should define "patients" broadly in this process and seek input from patients and family caregivers with lived experience with a specific disease state or therapeutic area, but also stakeholders who may not have that experience but who serve as patient advocates or are experts in issues such as health equity.

researchers assessing a treatment's value. The importance of including patient and clinician input in evidence-based processes has been underscored by a wide range of academics, thought-leaders, and research organizations. For example, in publishing its Rubric for patient-engagement, PCORI stated: "Engaging patients, caregivers, and other health care stakeholders as partners in planning, conducting, and disseminating research is a promising way to improve clinical decision-making and outcomes."¹⁶²

CMS recently published an ICR that includes "optional" submissions of data from Primary Manufacturers and the public regarding evidence about alternative treatments described in section 1194(e)(2).¹⁶³ Such information would need to be submitted no later than 30 days after publication of the selected drug publication list, would follow the questionnaire format of CMS' ICR, and would be in written format only. PhRMA is concerned that this regimented process will not be well-publicized or accessible to patient or clinician groups, when such input is essential to the MFP process. It is imperative that CMS gain relevant input early in the process and meaningfully consider it in determining specific MFPs. As previously noted, PhRMA also recommends that prior to making its initial offer to the manufacturer, CMS make available to the public key elements of its MFP analysis and provide an opportunity for the public to comment on them.

Clinician input will be particularly important for CMS to ensure that decision-making is rooted in the clinical reality of how selected drugs are used in a real-world clinical practice, and the drugs' impact on patients. CMS should specifically solicit advice from clinicians with experience specific to the relevant therapeutic area or disease state (e.g., if a treatment for Parkinson's disease is evaluated, a neurologist who specializes in Parkinson's disease or movement disorders should be consulted). Recent research found that estimates of value corresponding to assumptions identified by clinician-researcher experts and ICER often differed by substantial margins when examining the value of poly (ADP-ribose) polymerase (PARP) inhibitors in ovarian cancer. The differences found had a significant impact on results – utility estimates and treatment duration estimates yielded notable differences in the estimated value of the treatments.¹⁶⁴

These differences extend to assessments of a treatment's benefit compared to therapeutic alternative(s). A recently released study found that physicians in the U.S. disagreed with the German health agency's determination of the clinical benefit of innovative diabetes medicines 89 percent of the time. Of the U.S. physicians that disagreed, 97 percent said that the drugs in question provided additional clinical benefit for patients.¹⁶⁵ By including input from patients and relevant clinicians, CMS can help avoid discrepancies between how insurers or other price-setting agencies evaluate medicines versus how patients and clinicians value such medicines.

PhRMA recommends CMS consult with clinical leaders of the appropriate medical specialty societies, as well as leading clinical experts, during implementation of the Program and throughout the MFP determination process. This would include, at a minimum, key milestones, such as the scoping process for CMS' analysis, before the Agency makes an initial offer, and, if needed, in responding to a potential manufacturer counteroffer.

CMS has several options to facilitate input from clinicians in informal and formal manners. For example, CMS could convene ad hoc groups of clinicians and patients. In addition, CMS could establish a standing committee that provides input/recommendations, similar to the existing relationship between CMS and the American Medical Association (AMA), RVS Update Committee (RUC) or the Physician-Focused Payment Model

¹⁶² Sheridan S, Schrandt S, Forsythe L, Hilliard TS, Paez KA; Advisory Panel on Patient Engagement (2013 inaugural panel). (2017). The PCORI Engagement Rubric: Promising Practices for Partnering in Research. *Ann Fam Med*;15(2):165-170. DOI: 10.1370/afm.2042. PMID: 28289118; PMCID: PMC5348236.

¹⁶³ 54 Fed. Reg. 16983 (March 21, 2023).

¹⁶⁴ Cohen, J. T., Olchanski, N., Ollendorf, D. A., Neumann, P. J. (2022). The Certainty of Uncertainty in Health Technology Assessment. *Health Affairs Forefront*. Available at: <https://www.healthaffairs.org/doi/10.1377/forefront.20220125.37540/>.

¹⁶⁵ NAVLIN Insights. (2019). U.S. physicians disagree with Germany's determinations of the value of diabetes medicines. Eversana. Available at: <https://www.eversana.com/insights/u-s-physicians-disagree-with-germanys/>.

Technical Advisory Committee (PTAC).¹⁶⁶ Alternatively, particularly given the short timeframe before the first drugs are selected for price setting, CMS could also consider engaging an existing advisory committee, such as the Medicare Evidence Development and Coverage Advisory Committee (MEDCAC), as a resource in the MFP process.¹⁶⁷

Finally, following the statutorily required publication of the MFP explanation, PhRMA recommends CMS solicit feedback from all stakeholders regarding whether CMS has appropriately evaluated available evidence and arrived at an appropriate conclusion. This process will require CMS to ensure that the explanation provided after finalization of the MFP provides sufficient insight into CMS' decision-making process so that stakeholders are able to provide constructive and meaningful feedback.

j. Initial Justification

The written initial offer from CMS, which must be made no later than February 1st, 2024, must include a "concise" justification for the offer based on the negotiation factors and the methodology CMS lays out for developing an initial offer. The initial offer's justification is a critical part in the price setting process, particularly given the lack of communication between the manufacturer of the selected drug and the Agency that exists under CMS' proposed process. CMS must ensure that the initial justification enables the Primary Manufacturer to better understand the context for CMS' MFP offer, to inform the counteroffer and data provided as part of the counteroffer. As such, CMS needs to disclose all inputs and methodologies that it uses to arrive at an initial offer and must share this information prior to making the initial offer to ensure the manufacturer can properly respond to CMS.

PhRMA recommends that CMS describe, in final guidance, the template it will use for the concise justification and that it include information similar to the final published explanation and identify key pieces of information including:

- ***Therapeutic alternative(s) for a selected drug (for each indication);***
- ***How each of the factors listed in section 1194(e) were weighed relative to one another in CMS' decision-making;***
- ***Data and analysis CMS developed and considered supporting each factor, including evidence provided by third parties CMS engaged formally or informally;***
- ***Benefits and impacts of a selected drug CMS considered; and***
- ***Stakeholders, and other government agencies and organizations CMS engaged, formally or informally, including how stakeholder input explicitly informed CMS' determination of the MFP.***

k. Explanation for the MFP

CMS states that it will publish an explanation for the MFP no later than March 1st of the year prior to the IPAY year. For example, CMS will provide an explanation for the MFP for IPAY 2026 on March 1st, 2025. The intent of the published explanation is to summarize how the relevant factors were considered during the price setting process and would focus on the factors that had the greatest influence in determining the MFP. The published

¹⁶⁶ The RUC is a volunteer group of 32 physicians and other health care professionals who advise CMS regarding the valuation of a physician's "work" under the Medicare physician fee schedule. The PTAC is an 11-member group that provides comments and recommendations to the HHS Secretary on physician payment models.

¹⁶⁷ This advisory committee provides independent guidance and expert advice to CMS on specific clinical topics. MEDCAC is used to supplement CMS' internal expertise and has experience reviewing medical literature and technology assessments. The MEDCAC includes clinicians and patient advocates and could be a useful forum for CMS to convene in establishing the Program. CMS notes that it may recruit non-MEDCAC members who have relevant expertise to provide additional input to Committee members.

explanation will include high-level comments on the submitted data, without any proprietary information. The published explanation will list the selected drug, discuss contributing price setting factors, and note any factors or circumstances that may be unique to the selected drug. If the MFP is not agreed upon, CMS will indicate that no Agreement was reached.

PhRMA notes that for IPAY 2027, “Primary Manufacturers” will be required to submit manufacturer-specific data to CMS by March 1st, 2025, on the very same date such manufacturers have access to the explanation for how CMS arrived at the MFP for the prior year. This is an unworkable timeline. ***PhRMA strongly recommends that the MFP explanation be released simultaneously with the MFP and before the process to set prices for IPAY 2027 begins*** in order to give manufacturers essential predictability in CMS’ decision-making process. Manufacturers can better understand the process if they have access to the MFP explanation prior to being required to submit data to CMS for the following year. The statute requires CMS to publish the explanation *no later than* March 1st of the year prior to the IPAY, which indicates that CMS has discretion to publish the explanation at an earlier date. The published explanation of the MFP should be an important chance for CMS to solicit stakeholder feedback to improve the price setting process and is a critical piece in helping stakeholders understand how CMS arrives at an MFP for a selected drug. As this explanation could help build trust between CMS and other key stakeholders, ***PhRMA recommends the explanation provide information on many of the issues previously addressed, including but not limited to:***

- ***Therapeutic alternative(s) for a selected drug (for each indication);***
- ***How each of the factors listed in section 1194(e) were weighed relative to one another in CMS’ decision-making;***
- ***Data and analysis CMS developed and considered supporting each factor, including evidence provided by third parties engaged formally or informally by CMS;***
- ***Benefits and impacts of a selected drug CMS considered; and***
- ***Stakeholders and other government agencies and organizations CMS engaged, formally or informally, including how stakeholder input explicitly informed CMS’ determination of the MFP.***

As noted above, PhRMA also recommends that CMS offer manufacturers an opportunity to comment on a draft MFP explanation and that CMS respond to such comments.

I. Average Non-FAMP (Section 60.2.3)

Calculation of 2021 Annual non-FAMP

In section 60.2.3 of the Guidance,¹⁶⁸ CMS states that, in calculating the average 2021 non-FAMP for a selected drug, CMS intends to use the non-FAMP of each NDC-11 for the selected drug for each quarter of calendar year 2021. ***For the reasons discussed below, PhRMA instead recommends CMS to use the annual non-FAMP already reported by manufacturers to the VA as defined in 38 U.S.C. § 8126(h)(5).*** Specifically, for 2021, this would be the annual non-FAMP value reported by manufacturers to the VA by November 15, 2021.

In defining the average non-FAMP, the IRA does not specify which four quarters are “the 4 calendar quarters of the year involved” but notably cross-references 38 U.S.C. § 8126(h)(5). As noted above, 38 U.S.C. § 8126(h)(5) already defines an annual non-FAMP as a weighted average across the four quarters of the federal fiscal year, which runs from October through September of the following year. In defining the average non-FAMP for purposes of the IRA as based on a calendar year, CMS is introducing confusion, inefficiency, and added burden

¹⁶⁸ This approach is also proposed in section 60.2.1 with reference in section 50.1.

on both manufacturers and the Agency itself. Given the statutory reference to 38 U.S.C. § 8126(h)(5), CMS should instead utilize the existing annual non-FAMP as reported to the VA.

If CMS finalizes this portion of the guidance with the continued use of calendar year quarters, PhRMA supports the Agency's proposal for a weighted average.

Clarifying Weighting in Calculating a Single Average non-FAMP

In section 60.2.3 of the Guidance, CMS addresses its intended approach for calculating a single average non-FAMP across dosage forms and strengths of a selected drug for comparison against the calculated sum of the plan specific enrollment weighted amounts for the selected drug.

As written, the language included in the Guidance for steps 1 through 11 of section 60.2.3 could be read as utilizing units of NDC-11s used in the calculation of non-FAMP or units sold across all markets as opposed to units dispensed within the Part D program, which would result in an inconsistency with sections 60.2.2. and 60.5.

PhRMA urges CMS to clarify that the calculation of a single non-FAMP across dosage forms and strengths will be weighted by the 30-day equivalent supply dispensed under the Part D program as reported on the PDE. This would align the weighting methodology for the non-FAMP calculations with the weighting by 30-day equivalent supply utilized by CMS for the calculation of plan-specific enrollment weighted amounts in section 60.2.2 and the application of the single MFP across dosage forms and strengths in section 60.5.

Cross-Walking non-FAMP and PDE Unit Types

In step one of the calculation laid out in section 60.2.3 of the Guidance, CMS notes that the non-FAMP unit type may differ from unit types used on the Part D PDE record, which uses NCPDP-defined values. In such cases, CMS proposes to convert the non-FAMP unit type to the PDE unit type such that the average non-FAMP and the sum of plan specific enrollment weighted amounts represent the same quantity of the selected drug.

PhRMA agrees with the Agency on the need to convert non-FAMP units to PDE units in cases where the unit types differ for the same medicine. We would also encourage CMS to add a field to the PDE file layout to collect how the amount reported in the "Quantity Dispensed" field is measured using the NCPDP-defined values, as the Agency proposed in the Part D inflation rebate Guidance issued earlier this year.¹⁶⁹ Having this field added to the PDE would help CMS ensure accurate conversion of non-FAMP to PDE units, just as the Agency noted the potential of this field in helping to ensure accurate conversion of PDE to AMP units in the Part D inflation rebate Guidance.

m. Application of the MFP Across Dosage Forms and Strengths (Section 60.5)

In section 60.5 of the Guidance, CMS provides its intended approach to applying a single MFP across each dosage form and strength of a selected drug in accordance with section 1196(a)(2) of the Act. A key piece of this proposed approach (and indeed, a key piece of the methodologies CMS lays out in sections 60.2.2, 60.2.3, and 60.3 as well) rests on defining 30-day equivalent supplies for each dosage form and strength of a selected drug and therapeutic alternative(s).

PhRMA urges CMS to provide greater clarity regarding how the Agency intends to calculate 30-day equivalent supplies and identify alternative(s) when a 30-day supply cannot provide a reasonable comparison between therapeutic alternative(s). This calculation may not be as straightforward as it appears, particularly for certain types of medicines. Take the following two examples where CMS should give additional consideration to how to

¹⁶⁹ CMS. (February 9, 2023). Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of section 1860D-14B of SSA, and Solicitation of Comments. Available at: <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>

appropriately calculate 30-day equivalent supplies: (1) medicines used on an as-needed basis, such as rescue inhalers; or (2) when comparing two products where the treatment duration varies significantly (e.g., an oncology medicine that is administered on an ongoing basis until disease progression vs. a fixed-dose therapy) comparing the cost of a 30-day equivalent supply would not accurately capture the total cost of comparable outcomes. Medications where 30-day supplies can vary significantly across patients also need to be accounted for. For example, among patients using insulin, a typical 30-day supply can be very different from one patient to the next, both because different patients need different amounts of insulin, but also because insulin dosing varies by indication (e.g., for treatment for Type I vs. Type II diabetes). CMS should also give careful thought to how best account for starting dosages of medicines, where a patient's dosage increases over a period of time upon first starting a medication before reaching a steady, long-term dosage amount (e.g., titration).

PhRMA notes that manufacturers have experience with calculating 30-day equivalent supplies under certain state drug price transparency reporting requirements, and there are certain vendors that assist manufacturers with these calculations.¹⁷⁰ We suggest that CMS speak with manufacturers and these vendors to better understand how 30-day equivalent supplies are calculated for medicines, particularly medicines falling into one of the more complicated situations described in the paragraph above.

In addition to providing clarity on how the Agency intends to calculate 30-day equivalent supplies, PhRMA urges CMS to provide insight and data to manufacturers such that manufacturers can fully understand the Agency's application of a single MFP across dosage forms and strengths. Specifically, PhRMA requests that CMS make available to manufacturers of selected drugs:

- The Agency's calculated 30-day equivalent supply for each NDC-9;
- The total number of units dispensed for each NDC-9 in the 2022 Part D PDE data; and
- An Excel template with the Agency's 10-step calculation approach for applying the MFP across different dosage forms and strengths.

In providing this information to manufacturers of selected drugs, CMS will help to ensure that manufacturers have full transparency into the Agency's calculations.

n. Dispute Resolution

We are disappointed that CMS does not discuss mechanisms for dispute resolution, particularly after the Agency had indicated in its January 11, 2023 memo that "dispute resolution process for specific issues that are not exempt from administrative or judicial review under section 1198" would be one of seven major issues discussed in the Guidance.¹⁷¹ While the Agency references this in the introduction to the Guidance, it does not then describe any policy for resolving disputes or affording opportunities for manufacturers to engage with CMS to correct errors. Despite appeals mechanisms being widely recognized as a "best practice" for HTA-informed policy decision-making, CMS appears to be taking the position that provisions in SSA section 1198 preclude administrative and judicial review for many of the basic elements of the MFP program. PhRMA disagrees with any such interpretation of section 1198. Specifically, section 1198 does not prohibit CMS from establishing informal procedures to resolve disputes and affording manufacturers the opportunity to engage with the Agency to correct errors that will inevitably arise during the MFP decision-making process. Indeed, CMS interpreted similar statutory provisions on administrative and judicial review in connection with the Part B and Part D inflation

¹⁷⁰ For example, Global Pricing Innovations (<https://globalpricing.com/>).

¹⁷¹ CMS. (Jan. 11, 2023). Medicare Drug Price Negotiation Program: Next Steps on Implementation for Initial Price Applicability Year 2026. Available at: <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf>.

rebates to accommodate an error correction process.¹⁷² We were disappointed CMS chose not to put this discretion to use in the service of good public policy, as these opportunities to engage in meaningful dialogue to resolve disputes and correct errors would benefit both manufacturers and CMS and, importantly, could help avoid implementation missteps.¹⁷³ We encourage CMS to incorporate these processes into its final guidance for IPAY 2026.

Because the MFP program will involve CMS gathering and evaluating extensive and disparate types of cost and clinical data and research, and applying them to national MFP pricing decisions, it will create numerous potential areas where errors can occur or disputes arise over valid, but differing, assumptions (for example, interpretations on the appropriate approach to synthesizing data from different studies, or assumptions or extrapolations of treatment benefit based on study results). The risk of errors and disputes occurring will be further enhanced because the Agency will be required to conduct extensive evidence reviews in a much shorter time period than is typically required for traditional systematic reviews.¹⁷⁴

IV. Removal from the Selected Drug List Before or During Negotiation, or After an MFP is in Effect (Section 70)

For purposes of a selected drug's exit from the Program, "CMS will consider an approved generic drug or licensed biosimilar biological product to be marketed when [PDE] data reveal that the manufacturer of the generic drug or biosimilar biological product has engaged in bona fide marketing of that drug or product." As discussed in greater detail in our comments on section 90 below, there is no statutory basis for CMS' proposed "bona fide marketing" standard. Nevertheless, however CMS defines "marketing," CMS' timeline in section 70 for removing a selected drug is overly restrictive.

Specifically, CMS could read the law to allow a reference product to exit the Program if a generic or biosimilar product is marketed after the "negotiation period" but before the IPAY begins. Such reading aligns with the statutory definition of a (QSSD)—a threshold requirement for a drug to be subject to price setting. The statute defines a QSSD "with respect to an initial price applicability year,"¹⁷⁵ indicating that a product's status as a QSSD must exist as of the first day of the IPAY, not just at the selected drug publication date, as the Guidance suggests. Had Congress intended QSSD status to be assessed only as of the selected drug publication date, it would have said so. Thus, a product that has become multisource before the IPAY should not be subjected to price setting. This view also comports with the definition of "price applicability period," which means, "*with respect to a qualifying single source drug*, the period beginning with the first initial price applicability year with respect to which such drug is a selected drug and ending with the last year during which the drug is a selected drug."¹⁷⁶ This reference to QSSD status signals that a product that has gone multisource and hence no longer meets the QSSD definition should not be subject to a price applicability period. Moreover, as the statute and CMS' Figure 1 in the

¹⁷² CMS. (Feb. 9, 2023). Medicare Part B Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of section 1847A(i) of the Social Security Act, and Solicitation of Comments. Available at: <https://www.cms.gov/files/document/medicare-part-b-inflation-rebate-program-initial-guidance.pdf>; Available at: <https://www.cms.gov/files/document/medicare-part-b-inflation-rebate-program-initial-guidance.pdf> CMS. (Feb. 9, 2023). Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of section 1860D-14B of the Social Security Act, and Solicitation of Comments. Available at: <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>.

¹⁷³ Kelly, C. (2023). Medicare Price Inflation Rebate List Revisions a Sign of IRA Implementation Overload? Pink Sheet. Available at: <https://pink.pharmaintelligence.informa.com/PS148020/Medicare-Price-Inflation-Rebate-List-Revisions-A-Sign-Of-IRA-Implementation-Overload?vid=Pharma>.

¹⁷⁴ New York University Health Sciences Library. (2023). Systematic Reviews. NYU Langone Health. Available at: <https://hslguides.med.nyu.edu/systematicreviews/process>.

¹⁷⁵ SSA § 1192(e)(1).

¹⁷⁶ SSA § 1191(b)(2) (emphasis added).

Guidance show, only products that are QSSDs may be eligible drugs. Where a product is no longer a QSSD, it cannot, by definition, be considered an eligible drug or a selected drug.¹⁷⁷

Our position aligns with subsection (c)(1) in section 1192 and its use of the phrases, “with respect to the [IPAY]” and “with respect to such year” in paragraph (1).¹⁷⁸ This phrasing supports the conclusion that eligibility status (and hence, QSSD status) must remain in place as of January 1 of the IPAY for subsection (c)(1) to apply to the drug. Thus, this provision speaks to the exit process for drugs that remain a QSSD and selected drug on the first day of the IPAY and then experience generic or biosimilar competition. Paragraph (2) “clarif[es] the application of paragraph (1) to a specific time period when various tasks otherwise would need to be performed by both CMS and the manufacturer, i.e., during the negotiation period. The provision does not address what happens if the generic or biosimilar is marketed after the negotiation period, as there is no “negotiation process” to which the manufacturer is subject, and thus no need for a clarification that the process must stop. Paragraph (2)’s styling as a “clarification” shows that the underlying defined statutory terms referenced in subsection (c) must be given full effect in subsection (c)(1). In other words, it does not change the fact that the statute defines QSSD “with respect to an [IPAY].”

This position is grounded in sound policy. Congress crafted the IRA to provide for price setting for *single source* products. CMS’ current position undermines this intent by applying MFPs to products that are already multisource. This position thereby directly undermines generic and biosimilar competition and incentives for pursuing approval of these products. For generic and biosimilar companies, developing and marketing generic and biosimilar products within the timeframes under the law is already challenging. The processes necessary to market a generic or biosimilar product can be complex, and there are many steps that are not solely in control of the generic or biosimilar sponsor, including FDA review timelines. The MFP may go into effect before they are ever able to market their products and may set a price below the level of economic viability. CMS’ position compounds this problem by essentially providing that generic or biosimilar marketing in the last thirteen months before the IPAY does not trigger Program exit. In other words, a generic or biosimilar company that bring their products to the market during these thirteen months will nevertheless be forced to compete with an MFP.

We therefore urge CMS to revise the Guidance to provide that a reference product or listed drug exits the Program if generic or biosimilar marketing occurs after the negotiation period but before the IPAY. CMS also should amend the table on page 63 of the Guidance as follows.

¹⁷⁷ SSA § 1192(c) (defining “selected drug”), 1192(d) (defining “negotiation-eligible drug”).

¹⁷⁸ The section provides as follows:

(c) SELECTED DRUG.—

(1) IN GENERAL.—For purposes of this part, in accordance with subsection (e)(2) and subject to paragraph (2), each negotiation-eligible drug included on the list published under subsection (a) with respect to an initial price applicability year shall be referred to as a ‘selected drug’ with respect to such year and each subsequent year beginning before the first year that begins at least 9 months after the date on which the Secretary determines at least one drug or biological product—

(A) is approved or licensed (as applicable)—

(i) under section 505(j) of the Federal Food, Drug, and Cosmetic Act using such drug as the listed drug; or

(ii) under section 351(k) of the Public Health Service Act using such drug as the reference product; and

(B) is marketed pursuant to such approval or licensure.

(2) CLARIFICATION.—A negotiation-eligible drug—

(A) that is included on the list published under subsection (a) with respect to an initial price applicability year; and

(B) for which the Secretary makes a determination described in paragraph (1) before or during the negotiation period with respect to such initial price applicability year;

shall not be subject to the negotiation process under section 1194 with respect to such negotiation period and shall continue to be considered a selected drug under this part with respect to the number of negotiation-eligible drugs published on the list under subsection (a) with respect to such initial price applicability year.

Date on which CMS determines that a generic drug or biosimilar biological product is approved and marketed	Result with respect to selected drug for the Program
September 1, 2023 through August 1, 2024 <u>December 31, 2025</u> (which includes Negotiation Period for initial price applicability year 2026)	Selected drug remains a selected drug for initial price applicability year 2026, though MFP does not apply; selected drug ceases to be a selected drug on January 1, 2027
August 2, 2024 <u>January 1, 2026</u> through March 31, 2026	Selected drug remains a selected drug and MFP applies for initial price applicability year 2026; selected drug ceases to be a selected drug on January 1, 2027.
April 1, 2026 through March 31, 2027	Selected drug remains a selected drug and MFP applies for initial price applicability year 2026 and calendar year 2027; selected drug ceases to be a selected drug on January 1, 2028.

V. Manufacturer Compliance and Oversight (Section 90)

a. Monitoring of Access to the MFP (Section 90.2)

Please refer to our comments on section 40.4 for a discussion of CMS’ proposals in section 90.2 of the Guidance.

b. Monitoring for Bona Fide Marketing of Generic or Biosimilar Product (Section 90.4)

“Bona Fide Marketing”

With respect to section 90.4, even accepting for the sole purpose of commenting on this Guidance that CMS’ adoption of a “bona fide marketing” standard is final, there is nevertheless no statutory basis for CMS’ proposal “to monitor whether robust and meaningful competition exists in the market once it makes such a determination [that a generic drug or biosimilar biological product has been marketed].”¹⁷⁹ The statute contemplates that a selected drug will exit the program based on such a determination and nothing more, and does not provide CMS a role in monitoring generic and biosimilar competition. As set out below, CMS’ concept of “bona fide marketing” is contrary to the statute. This approach also fails to provide clarity or certainty regarding when a medicine becomes ineligible for price setting.

The statute defines a QSSD in relevant part as a drug for which a generic or biosimilar product is not “marketed.”¹⁸⁰ The guidance instead refers to a new term “bona fide marketing,” providing that, “[i]n accordance with 1192(c) and (e) of the Act for the purpose of identifying [QSSDs] for [IPAY] 2026, CMS will review PDE data for a given generic drug or biosimilar . . . and will consider a generic drug or biosimilar biological product to be marketed when that data reveal that the manufacturer of that drug or product has engaged in bona fide

¹⁷⁹ Guidance, p. 67.

¹⁸⁰ SSA § 1192(e)(1)(A)(iii) & (B)(iii); *see also id.* § 1192(c)(1)(B) (addressing the termination of “selected drug” status following the Secretary’s determination that a generic or biosimilar product “is marketed.”).

marketing of that drug or product.”¹⁸¹ The addition of the term “bona fide” adds an extra-statutory limitation and is at odds with the ordinary meaning of “marketed.”

Indeed, in the guidance’s “Appendix C: Definitions for Purposes of Collecting Manufacturer-Specific Data,” CMS defines “marketing” as “the introduction or delivery for introduction into interstate commerce of a drug product.”¹⁸² PhRMA agrees with this definition, which is consistent with FDA’s interpretation of provisions of the FDCA for which a product’s marketing status is relevant. For example, in the context of 180-day exclusivity for first generic applicants, the FDCA provides that FDA shall not make effective a subsequent generic application until “180 days after the date of the first commercial marketing of the drug...by any first applicant.”¹⁸³ In regulations, FDA defines the term “commercial marketing” in relevant part as “the introduction or delivery for introduction into interstate commerce of a drug product described in an ANDA, outside the control of the ANDA applicant.”¹⁸⁴ This definition is particularly relevant given that the IRA specifically refers to the generic product being “marketed under section 505(j) of the [FDCA],” which has long been understood to mean introduction into interstate commerce.¹⁸⁵ Had Congress intended to change the criteria for a generic to be considered “marketed,” it would have done so. Similarly, for purposes of implementing section 506I of the FDCA concerning marketing status reports, FDA considers a product’s marketing status to depend on whether a product is distributed by the application holder, i.e., whether the product is available for sale.¹⁸⁶ Notably, since the IRA’s enactment, Congress extended the section 506I marketing provisions to apply to biologics licensed under the PHSA and in so doing made no changes that would suggest Congress meant to do anything other than endorse FDA’s approach to defining marketing status.¹⁸⁷ FDA’s definitions reflect the generally accepted ordinary meaning of the “marketing” of a pharmaceutical product, and, consequently, the meaning of “marketed” that Congress intended in the context of the IRA. Moreover, in a Supreme Court case involving a law that used the term “marketing,” but left the term “undefined,” the Court used “ordinary meaning” of “marketing.”¹⁸⁸ Significantly, the Court held that “[m]arketing ordinarily refers to the act of holding property for sale with the activities preparatory thereto . . . and does not require that the promotional or merchandising activities connected with the selling be extensive.”¹⁸⁹ In contrast, the guidance imposes an extra-statutory limitation on qualifying marketing that goes beyond its ordinary meaning. *We urge CMS to abandon the new term “bona fide marketing” and rely instead on the definition of “marketing” in Appendix C.*

CMS’ position also conflicts with another part of the Program statute at section 1192(f)(2)(D)(iv) which expressly prohibits manufacturers from receiving the biosimilars-based selection “pause” based on volume-limited arrangements. Specifically, section 1192(f)(2)(D)(iv) states that “[i]n no case shall the Secretary delay the inclusion of a biological product as a selected drug on the list published under subsection (a) if the Secretary determined that the manufacturer of the biosimilar...entered into any Agreement described in such paragraph with the manufacturer of the reference product...that...*restricts the quantity (either directly or indirectly) of the biosimilar biological product that may be sold in the United States over a specified period of time.*”¹⁹⁰ Clearly, then, Congress knew how to impose volume-based requirements or limitations and did so in the very same section of the statute. Again, when “Congress includes particular language in one section of a statute but omits it in another section of the same Act,” it is “generally presumed that Congress acts intentionally and purposely in the

¹⁸¹ Guidance, p. 10.

¹⁸² Guidance, p. 82.

¹⁸³ FDCA § 505(j)(5)(B)(iv)(I).

¹⁸⁴ 21 C.F.R. § 314.3.

¹⁸⁵ *Id.*

¹⁸⁶ See FDA, Guidance for Industry, *Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act: Content and Format*, at 3 (Aug. 2020) (describing the discontinuation of marketing a product as ceasing distribution); see also FDCA § 506I (describing reporting requirements relating to marketing status).

¹⁸⁷ Consolidated Appropriations Act, 2023, Pub. L. No. 117-328, § 3201 (2022).

¹⁸⁸ *Asgrow Seed Co. v. Winterboer*, 513 U.S. 179, 187–88 (1995).

¹⁸⁹ *Id.* (emphasis added).

¹⁹⁰ SSA § 1192(f)(2)(D)(iv) (emphasis added).

disparate inclusion or exclusion.”¹⁹¹ Congress’s decision not to qualify the term “marketed” demonstrates that CMS’ additional “bona fide” limitation conflicts with the statute.

The use of specific PDE data and the time frame for such data, as described in the Guidance, are also at odds with the statutory language. The guidance states that “CMS will review PDE data for a given generic drug or biosimilar biological product during the 12-month period beginning August 16, 2022 and ending August 15, 2023, using PDE data available on August 16, 2023, and will consider a generic drug or biosimilar biological product when that data reveal that the manufacturer of that drug or product has engaged in bona fide marketing of that drug or product.”¹⁹² The statute does not instruct CMS to consider PDE data – either exclusively, or at all – in assessing marketing status and to ignore all other sources of marketing information. Thus, in accordance with the statute, the determination of whether a product is marketed, as that term is commonly understood, should not be based on PDE data.

PDE data are inappropriate as a benchmark to assess whether a generic or biosimilar is marketed. PDE data only reflect Part D claims: Part D plans are a subset of payors, which themselves are a subset of the biopharmaceutical marketplace, and a subset that would be expected to pay for a newly approved drug later than other segments of the marketplace. And in fact, Medicare Part D plans are “notably slower than commercial plans in coverage of first generics... For the 2021 Medicare Part D plan year, on average, only 21 percent of first generics that launched in 2020 were covered by plan formularies.” An analysis by the Association for Accessible Medicines found that “it takes nearly three years before first generics are covered on more than half of Medicare Part D formularies,” and even when covered, these drugs are less likely to be placed on generic tiers (meaning that the generic may be infrequently used and thus may not appear in any particular sample of PDE data even if it is covered by the Part D plan).¹⁹³ This delayed utilization pattern – even for first generics – is consistent with the fact that CMS allows Part D plans’ Pharmacy and Therapeutics Committees a lengthy period to review new drugs and decide whether to place them on formulary.¹⁹⁴ In short, hinging a decision about when a new generic or biosimilar is “marketed” solely on records of Part D utilization is an arbitrary and irrational approach that inevitably will miss most of the evidence of marketing and determine an incorrect date for when marketing of the drug began.

Finally, any monitoring by CMS of the competitive landscape for pharmaceuticals would duplicate the existing efforts of the Federal Trade Commission (FTC), which has the statutory authority and expertise to perform this function. It is also unnecessary in light of FDA initiatives, including the Drug Competition Action Plan¹⁹⁵ and Biosimilars Action Plan,¹⁹⁶ which have focused on improving access to generic and biosimilar products in the U.S. Moreover, the FTC and FDA have also been working together on these issues, issuing joint statements and holding joint workshops, most recently focusing on competition for biologics and biosimilars.¹⁹⁷ CMS also lacks the expertise and resources to police marketplace competition issues. CMS’ proposed monitoring of the status of competition in the marketplace therefore is unauthorized and unnecessary.

¹⁹¹ *Russello v. United States*, 464 U.S. 16, 23 (1983) (citations omitted).

¹⁹² Guidance, p. 10.

¹⁹³ New Generics are Less Available in Medicare than Commercial Plans, AAM at 5-6. (July 2021). Available at: <https://accessiblemeds.org/sites/default/files/2021-07/AAM-New-Generics-Are-Less-Available-in-Medicare-2021.pdf> at 5, 6. See also Appendix at p. 10 (showing that generic uptake in Medicare dipped as low as 12 percent for generics launched in 2017).

¹⁹⁴ Medicare Prescription Drug Benefit Manual, chap. 6, section 301.5 (Part D plans’ P&T committees should generally make a “reasonable effort” to review a newly-approved drug within 90 days and decide whether to add the drug to the plan formulary within 180 days, or provide a “clinical justification” if this timeframe is not met); section 30.2.5 (even for new drugs in the Part D six protected classes, plan P&T committees have 90 days to review the new drug and add it to the plan formulary).

¹⁹⁵ FDA Drug Competition Action Plan. Available at: <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/fda-drug-competition-action-plan>.

¹⁹⁶ FDA Biosimilars Action Plan: Balancing Competition and Innovation. Available at: <https://www.fda.gov/media/114574/download>.

¹⁹⁷ FDA and FTC Collaborate to Advance Competition in the Biologic Marketplace. Available at: <https://www.fda.gov/news-events/fda-voices/fda-and-ftc-collaborate-advance-competition-biologic-marketplace>.

VI. Civil Monetary Penalties (Section 100)

In section 100 of the Guidance, CMS addresses the civil monetary penalty (CMP) provisions set forth in section 1197 of the SSA (the Program-related CMPs) and briefly describes the “procedures” CMS intends to follow to impose these CMPs on manufacturers. Our comments reflect how we believe CMS can implement these CMPs in a manner that conforms to the statute, while affording reasonable and appropriate protections to manufacturers.

a. Notice-and-Comment Rulemaking on Program-Related CMPs

The extraordinary nature of Program-related CMPs demands notice-and-comment rulemaking. Section 1197 authorizes extraordinarily high CMP amounts. To our knowledge, the maximum CMP amount set forth in section 1197(d), which provides for a penalty equal to \$100 million for each item of false information, is *by far* the highest CMP amount related to any federal health care enforcement regime. Moreover, the maximum CMP amount set forth in section 1197(a) is equal to 10 times the difference between the price the manufacturer charges and the MFP¹⁹⁸ – a strikingly large amount in comparison to the most common punitive fine recognized in American law (*i.e.*, treble damages). Further, the maximum CMP amount set forth in section 1197(c) of \$1 million per day greatly exceeds other “per-day” CMP amounts in the SSA (such as the maximum \$10,000 per day penalty in section 1927(b)(3)(C)(i) for the similar failure of a manufacturer to provide timely information relevant to Medicaid drug rebates).

These extraordinarily high penalties, by themselves, warrant notice-and-comment rulemaking prior to Agency implementation. When coupled with the complexity and novelty of the Program and the implementation challenges that will persist for at least the first few years, basic notions of fairness and due process require notice-and-comment rulemaking. PhRMA strongly urges CMS to complete this notice-and-comment process before seeking to impose any Program-related CMPs on a manufacturer. Such rulemaking should address the following issues, at a minimum:

- Clear and detailed procedures CMS intends to use to impose Program-related CMPs against selected drug manufacturers;
- The scope of a selected drug manufacturer’s Program-related CMP liability with respect to acts and omissions of third parties, including independent actors in the pharmaceutical supply chain over which the manufacturer exercises little, if any, control; and
- Factors CMS will consider in assessing whether to seek a Program-related CMP and the amount of any such CMP.

We address each of these issues, in turn, below.

b. Combined Rulemaking on CMP Procedures

PhRMA urges CMS to implement IRA drug pricing-related CMP procedures through a single rulemaking and model such procedures after well-established precedents. Given the significant overlap between the CMP provisions in sections 1197 (governing the Program), 1847A(i)(7) (governing Part B rebatable drugs), and 1860D-14B(e) (governing Part D rebatable drugs) of the SSA, PhRMA urges CMS to undertake notice-and-comment rulemaking to implement a common set of procedures to govern these CMPs.¹⁹⁹ We note that proceeding through notice-and-comment rulemaking to implement procedures for these CMPs would be consistent with CMS’

¹⁹⁸ A similar penalty amount applies with respect to a manufacturer’s failure to pay a rebate due in connection with the biosimilar delay provisions. *See* SSA § 1197(b).

¹⁹⁹ To clarify, CMS should codify separate regulatory provisions to address the circumstances under which a manufacturer could be subject to a CMP under: (1) the Program; (2) the Part B inflation rebate program, and (3) the Part D inflation rebate program. These separate regulatory provisions should cross-reference a single CMP appeals procedure that applies to all IRA drug pricing-related CMPs.

obligation under section 1871(a) of the SSA to issue regulations before establishing a substantive legal standard.²⁰⁰

In developing procedures to govern the imposition of CMPs, CMS should use well-established agency procedures as a model. Examples include the CMP procedures for Medicare Advantage organizations (MAOs) and Part D prescription drug plan sponsors (PDPs),²⁰¹ and the CMP procedures issued by the HHS OIG.²⁰² Each of these examples establishes clear and detailed procedures for the Agency to provide detailed notice of the basis of the CMP and for the regulated parties to, among other things, respond to CMP notices, request hearings before an administrative law judge (ALJ), and appeal ALJ decisions to the HHS Departmental Appeals Board before seeking review in the U.S. Court of Appeals.²⁰³

In addition, the CMP procedures should provide an opportunity for manufacturers to confer with the Agency prior to the imposition of CMPs. Even when regulations do not require it, it is customary for government agencies to issue pre-enforcement notification letters or pursue other informal means to give regulated parties an opportunity to respond before the Agency initiates formal proceedings, such as by issuing a CMP notice.²⁰⁴ Engaging in pre-enforcement discussions with manufacturers would be beneficial to both manufacturers and CMS. This is particularly true because of the extraordinarily high CMP amounts at issue and the novelty and complexity of the Program, which is still being implemented. Both manufacturers and CMS will likely be working through implementation challenges, often fact-specific, for at least the first few years of the Program. Therefore, it is critical that CMS implement a process to informally engage with manufacturers through pre-enforcement communications before initiating formal CMP proceedings.

c. CMPs Due to Acts and Omissions of Third Parties

PhRMA urges CMS to not impose CMPs on drug manufacturers for acts and omissions of third parties over which manufacturers have little, if any, control. As reflected earlier in our comments, PhRMA strongly opposes CMS' intention to hold a Primary Manufacturer responsible for certain acts and omissions of a Secondary Manufacturer. PhRMA is deeply concerned that, under this framework, CMS could attempt to impose \$1 million-per-day CMPs on a Primary Manufacturer for acts or omissions of a Secondary Manufacturer over which the Primary Manufacturer has little, if any, control.²⁰⁵

Similarly, CMS intends to hold Primary Manufacturers "ultimately" "responsib[le]" for ensuring access to the MFP, despite acknowledging that "[e]ach component of the pharmaceutical supply chain may have a role in making the MFP available to MFP-eligible individuals."²⁰⁶ Here, too, manufacturers have very limited, if any, ability to influence the conduct of independent actors in the pharmaceutical supply chain. Notwithstanding these

²⁰⁰ In any event, under section 1847A(i)(7) of the SSA, CMS is expressly required to issue regulations establishing procedures governing CMPs under the Medicare Part B inflation rebate program.

²⁰¹ 42 C.F.R. Part 422, Subparts O and T (CMP procedures for MAOs); 42 C.F.R. Part 423, Subparts O and T (parallel procedures for PDPs).

²⁰² 42 C.F.R. Parts 1003 and 1005.

²⁰³ We note that the limitations on administrative and judicial review set forth in section 1198 of the SSA do not limit a manufacturer's right under section 1128A(e) of the SSA to seek judicial review of a determination by the Secretary to impose a CMP pursuant to section 1197.

²⁰⁴ See, e.g., OIG, Revisions to the OIG's Exclusion Authorities, 82 Fed. Reg. 4100, 4109 (Jan. 12, 2017) ("In practice, OIG also contacts potential subjects of section 1128(b)(7) exclusions, often through 'pre-demand letters' or other means to give defendants the opportunity to respond to OIG before formal proceedings are initiated."); 42 C.F.R. §§ 422.756, 423.756 (setting forth CMS' procedure for imposing intermediate sanctions on MAOs and PDPs, respectively, which provides for a written notice to the plan of CMS' proposed intermediate sanction and an opportunity for the plan to provide a written rebuttal within 10 days of receipt of CMS' notice).

²⁰⁵ For example, it appears from the guidance that CMS believes it could impose \$1 million-per-day CMPs on a Primary Manufacturer in the following instances: (1) a Secondary Manufacturer fails to make the MFP available to MFP-eligible individuals or specified dispensers, see, e.g., Guidance at 26, 68-69; and (2) a Secondary Manufacturer fails to provide a Primary Manufacturer with required non-FAMP information for a selected drug that the Primary Manufacturer would be required to submit to CMS for purposes of the "negotiation," see, e.g., Guidance, pp. 27-28, 69.

²⁰⁶ Guidance, p. 65.

limitations, the Guidance suggests manufacturers could face CMPs equal to 10 times the difference between the net acquisition price and the MFP *for each unit* of a selected drug acquired at a price exceeding the MFP.²⁰⁷

PhRMA strongly opposes any interpretation of the statute that would seek to impose CMP liability on manufacturers of selected drugs due to the acts or omissions of any independent third party. Doing so would dramatically expand the scope of manufacturers' legal liability and disrupt the allocation of risk under numerous contractual arrangements between and among manufacturers and other entities spanning the pharmaceutical supply chain. Amending these contracts to account for CMS' policy change would require significant time and resources that CMS does not address in setting forth these new compliance expectations for manufacturers.

While PhRMA strongly opposes CMS' intention to shift legal risk to manufacturers in this manner, if CMS retains these policies in the final IPAY 2026 guidance, the Agency should *at a minimum* articulate a non-enforcement policy pursuant to which it will refrain from imposing CMPs on Primary Manufacturers under sections 1197(a) and 1197(c) for a reasonable time following issuance of the final guidance for IPAY 2026.²⁰⁸ In addition, as discussed below, if CMS pursues CMPs against any Primary Manufacturer based on a third party's conduct, CMS should weigh the Primary Manufacturer's level of culpability to seek a low penalty.

d. CMS Explanation of Factors Used in Assessing CMPs

CMS should publicly explain the factors it will consider in assessing CMPs against manufacturers. As a threshold matter, the extraordinary maximum penalty amounts for the Program-related CMPs present serious concerns under the Excessive Fines Clause of the Eighth Amendment to the U.S. Constitution. While these amounts are set by statute, in seeking to impose a CMP on a manufacturer, CMS should consider whether a compromise penalty amount below the statutory amount is required to avoid this constitutional issue.²⁰⁹

Moreover, given the extraordinary range of potential penalty amounts under the statutory maximums, PhRMA strongly urges CMS to clearly explain, through notice-and-comment rulemaking, the factors it will consider and weigh in assessing whether to seek a Program-related CMP and the amount of any such CMP. CMS has clear statutory authority to exercise such discretion. Specifically, each Program-related CMP cross-references section 1128A of the SSA, which requires that, in determining the amount of any CMP, agencies must consider "the nature of claims and the circumstances under which they were presented, "...the degree of culpability, ...[and] such other matters as justice may require."²¹⁰

Factors CMS should consider as part of this rulemaking include, for example:

- the nature and circumstances of the manufacturer's conduct;
- the degree of the manufacturer's culpability, including, for example, whether the manufacturer took timely and appropriate corrective action;
- whether the manufacturer had knowledge of a violation of an applicable Program requirement;
- the clarity of existing guidance available to the manufacturer;

²⁰⁷ Guidance, pp.64-65, 68.

²⁰⁸ We note that there is precedent for this approach. For example, OIG proposed adopting a similar policy of enforcement discretion in its 2020 proposed rule on CMPs related to information blocking. *See* 85 Fed. Reg. 22979, 22985 (Apr. 24, 2020) ("We appreciate that information blocking is newly regulated conduct...The goal in exercising our enforcement discretion is to provide individuals and entities that are taking necessary steps to comply with the ONC Final Rule with time to do so while putting the industry on notice that penalties will apply to information blocking conduct within a reasonable time.").

²⁰⁹ SSA § 1128A(f) authorizes agencies to "compromise" CMPs imposed on regulated parties.

²¹⁰ SSA § 1128A(d).

- efforts by the manufacturer to obtain clear guidance from CMS and/or another government Agency on a specific issue impacting the manufacturer’s compliance with an applicable Program requirement;
- good faith efforts by the manufacturer to comply with applicable Program submission deadlines (*e.g.*, submission of information pursuant to section 1193(a)(4)), considering reasonable requests by the manufacturer that CMS extend such deadlines in appropriate circumstances; and
- the degree to which a manufacturer could exercise control over, or sought to address the conduct of, a third party on which a manufacturer relied in satisfying an applicable Program requirement.

CMS’ discussion of how it will consider and weigh these factors should provide clear, detailed, and meaningful distinctions in penalty amounts to help manufacturers focus compliance efforts consistent with CMS priorities. In light of ongoing implementation of the Program, which will continue for at least a few years, CMS should construe the foregoing factors liberally in favor of manufacturers and in a manner that would not trigger a CMP. Such an approach is particularly appropriate where a manufacturer has engaged with CMS in good faith and can demonstrate that it has taken reasonable steps to comply with applicable Program requirements.

e. Threshold for Manufacturer CMP Liability

Program CMPs that require a manufacturer to act “knowingly” should apply only if the manufacturer had actual knowledge. Section 1197(c) of the SSA is the only CMP provision that requires a manufacturer to act “knowingly” for liability to attach. Specifically, a manufacturer must knowingly provide false information under certain procedures that apply in connection with the small biotech exception or the biosimilar delay provisions. A manufacturer that knowingly submits such information is subject to a CMP equal to \$100 million for each item of false information.

Separately, in section 100.2 of the Guidance, CMS states that a manufacturer would be out of compliance with the requirement to submit information under section 1193(a)(4) of the SSA and subject to a CMP equal to \$1 million per day of a violation under section 1197(c) if it knowingly submits false information required under the Agreement between the manufacturer and CMS.

CMS should not attempt to impose a CMP on a manufacturer under either of these provisions unless CMS can first demonstrate that the manufacturer had actual knowledge of a violation. Importantly, the term “knowingly” is not defined in Part E of Title XI of the SSA. Nor is the term defined in section 1128A of the SSA, which is incorporated by reference into the Program-related CMPs.²¹¹ In the absence of a legally binding definition of “knowingly,” CMS should interpret this term based on its plain meaning, which requires one to act “[w]ith knowledge; consciously; intelligently.”²¹² The extraordinary amounts of these CMPs further support interpreting “knowingly” in its most natural way to reserve such penalties for only truly knowing conduct. Accordingly, CMS should not seek to impose a CMP under either of these provisions unless CMS can first demonstrate that the manufacturer had actual knowledge of a violation.

VII. Part D Formulary Inclusion of Selected Drugs (Section 110)

In section 110 of the Guidance, CMS notes that “Medicare Part D plans shall include each covered Part D drug that is a selected drug on Part D formularies during Contract Year (CY) 2026 and all subsequent years for which the MFP of the selected drug is in effect during the price applicability period.” PhRMA agrees with CMS that, per the statute, any drug that is a selected drug, for which the MFP is in effect, must be on all Part D formularies and widely available to beneficiaries in Medicare.

²¹¹ The Program-related CMPs incorporate the definitions and all other procedural aspects of section 1128A. Only the substantive violations described in subsections (a) and (b) are not incorporated.

²¹² Black’s Law Dictionary, Knowingly, <https://thelawdictionary.org/knowingly/> (accessed Mar. 26, 2023).

PhRMA also would like to note our concerns that price setting, layered on top of the significant changes in stakeholder liability from Part D redesign, will have significant impacts on the structure of Part D and could negatively impact patient access to medicines. Indeed, we believe that price setting will put the very nature of Part D's competitive system at risk. Negotiations between plans and manufacturers around formulary and benefit designs are foundational elements of Part D's current market-based system, which has delivered broad access for beneficiaries to a range of plans and treatment options since the program's inception. The Agency must tread carefully in implementing the IRA and setting prices for selected drugs so that these foundational program elements are not completely undermined and beneficiary access to medicines is not lost or hindered.

As described in more detail below, the price setting in the IRA will have impacts far beyond the drugs selected for IPAY 2026, extending to other therapeutic competitors in the class. To that end, ***PhRMA recommends that CMS' process for arriving at a final MFP for selected medicines should seek to minimize effects within therapeutic classes that would result in narrower formularies and fewer choices for patients. CMS should also be mindful and seek to limit the risk of perverse incentives that are more likely to result from MFPs set at levels well below the ceiling price.*** CMS should create sufficient safeguards to ensure that there is diversity across plan formularies to offer beneficiaries plan options that continue to meet their individual therapeutic needs. In practice, this calls for plan formularies that include both selected drugs and medicines that aren't subject to government price controls.

To illustrate these concerns, recent analysis by the Hayden Consulting Group of the impact of the IRA's government price setting provisions on the Part D program show that the market-based competitive conditions that have led to historical access for a broad array of treatments in Part D could be stifled.²¹³ Specifically, Hayden examines illustrative therapeutic classes where there is significant brand-to-brand competition today and evaluates changes in plan liability before and after implementation of the IRA, assuming that at least one competitor in the class is subject to price setting. To limit an increase in liability and mitigate risk, Hayden concludes that plans are likely to impose aggressive utilization management to limit market share for medicines that are not subject to price setting, and/or demand higher rebates for formulary access.²¹⁴ Hayden's analysis assumes that these formulary dynamics occur when the MFP is set at the ceiling price and notes the "magnitude of the MFP discount will be the greatest determinant of competitive dynamics in the market."²¹⁵ To the extent that CMS sets MFPs for selected drugs well below the ceiling these potential formulary dynamics could intensify further.

As the IRA is implemented, Part D's broad choice of medicines must be maintained. CMS' MFP process should have as a key goal expanded access to medicines for Medicare beneficiaries – including coverage, access, and affordability that is as good as or better than what is in place today – rather than more restrictions in coverage. To that end, ***PhRMA recommends that CMS review and update its formulary review standards*** to reflect the significant shift from the competitive environment that has been in place since the Part D program's inception to today, recognizing the IRA's major changes to the Part D benefit as a result of redesign and government price setting for a steadily growing number of medicines over time. ***PhRMA specifically recommends that CMS pay close attention to plans' tiering decisions, cost-sharing levels, patient out-of-pocket exposure, and utilization management protocols for both brand and generic medicines to ensure that plans do not over-emphasize low premiums at the expense of enrollees having high quality benefits that provide affordable access to medicines.***

Given major changes in the Part D program occurring in the coming years, Part D plans are also likely to expand upon current trends towards more formulary tiers and increase the number of medicines subject to maximum

²¹³ Hayden Consulting Group. (Oct 31, 2022). Government Price Negotiation & its Anticipated Impact on Contracting Dynamics in Medicare Part D. Available at: <https://www.haydencg.com/post/hcg-white-paper-series-the-inflation-reduction-act>.

²¹⁴ Hayden Consulting Group. (Nov 10, 2022). Government Price Negotiation & its Anticipated Impact on Contracting Dynamics in Medicare Part D. Available at: <https://www.haydencg.com/post/hcg-white-paper-series-the-inflation-reduction-act-3>.

²¹⁵ Hayden Consulting Group. (Dec 20, 2022). Inflation Reduction Act: Impact of the DNP & Future Dynamics, including Medicare Part B. Available at: <https://www.haydencg.com/post/hcg-white-paper-series-the-inflation-reduction-act-4>.

coinsurance requirements, continuing to stratify their formularies and increasing the number of medicines placed on non-preferred and specialty tiers. According to MedPAC's most recent report to Congress, in 2019 most Part D beneficiaries were enrolled in plans that utilized a five-tier formulary, including a specialty tier for medicines exceeding a certain cost threshold, and the use of coinsurance was widespread.²¹⁶ Additional formulary tiers can result in access burdens for patients, as Part D plan sponsors typically impose up to 33 percent coinsurance for medicines on the specialty tier, and coinsurance for non-preferred tier medicines can be as high as 40 to 50 percent.²¹⁷

Patient out-of-pocket burdens are exacerbated by current practices of Part D plan sponsors to retain the substantial discounts and rebates negotiated with manufacturers, typically using rebate dollars to reduce premiums overall instead of lowering patient cost sharing on rebated medicines. Even if a Part D sponsor or its PBM has negotiated a rebate for a medicine, beneficiary coinsurance is typically based on a medicine's undiscounted list price. A recent analysis found that 92 percent of Part D beneficiaries' out-of-pocket spending is based on the list price rather than the discounted price their insurer gets.²¹⁸ For beneficiaries with coinsurance, failure to pass through rebates at the point-of-sale could manifest in disproportionately high out-of-pocket costs for non-selected drugs. This is because while selected drugs will have their coinsurance calculated as a percentage of the MFP price, coinsurance for competing non-selected drugs will continue to be based on the undiscounted price of the drug, even in cases when the manufacturer provides a substantial rebate. To address the out-of-pocket challenges caused by plans' and PBMs' failure to pass rebates directly to patients at the point-of-sale, ***PhRMA recommends that CMS redefine Part D negotiated price to take into account all manufacturer price concessions.***

PhRMA also recommends that CMS update its plan evaluation and oversight procedures and rigorously exercise its responsibility to enforce statutory non-discrimination requirements in Part D. Specifically, PhRMA urges CMS to conduct diligent formulary oversight to guard against increasingly aggressive utilization management restrictions or the narrowing of patient treatment options, including exclusion of medicines. In particular, CMS should increase transparency of the Agency's formulary review processes, reporting on CMS' oversight and outcomes of the formulary reviews outlined in the Part D Benefits Manual.²¹⁹ Since Part D's origination, plans have increasingly restricted access to medicines in Part D through tighter formularies, limiting the number of medicines covered for beneficiaries. Additionally, insurers use utilization management as a strategy to reduce their spending on covered medicines, which can have a negative impact on patient access. These insurance tactics, including prior authorization and fail first (also known as step therapy), may prevent or delay patients from accessing the medicines prescribed by their physicians. A recent report from GoodRx found that the average number of medicines covered by Part D that are subject to utilization management

²¹⁶ MedPAC. (March 2019). Report to the Congress: Medicare Payment Policy. Chapter 14. Available at: https://www.medpac.gov/wp-content/uploads/import_data/scrape_files/docs/default-source/reports/mar19_medpac_ch14_sec.pdf

²¹⁷ Cubanski J, Damico A, Neuman T. (May 2018). Medicare Part D in 2018: The Latest on Enrollment, Premiums and Cost-Sharing. Kaiser Family Foundation.

²¹⁸ PhRMA. (March 2021) "Trends in Out-of-Pocket Spending for Brand Medicines in Medicare Part D." Available at: https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/S-U/Trends-in-Out-of-Pocket-Spending-for-Brand-Medicines-in-Medicare-Part-D_FINAL-Update-May-21.pdf.

²¹⁹ Section 30.2.7 (Formulary Performance and Content Review) of the Part D benefits manual, outlines CMS' key formulary review concepts which include: review of tier placement to ensure the formulary doesn't discourage enrollment of certain beneficiaries, determining whether appropriate access is afforded to drugs or drug classes addressed in widely accepted treatment guidelines, availability of the most commonly prescribed drug classes for the Medicare population, and review of UM restrictions to ensure that use of these tools are consistent with industry best practices and identification of outliers. CMS should more clearly define these standards such as what it means for a formulary to provide "appropriate access" and for UM restrictions to be "consistent with industry best practices" or "outliers." Additionally, CMS should issue an annual report providing aggregate data on the analyses it conducted, the results of those analyses, and changes to formularies and UM required by its analyses. Reporting should be sufficiently specific to allow stakeholders and researchers to assess the impact of CMS' formulary review on formulary design and patient access to medicines. Transparency into the findings of these formulary reviews are critical to understanding patient safeguards to access. Available at: <https://www.cms.gov/medicare/prescription-drug-coverage/prescriptiondrugcovcontra/downloads/part-d-benefits-manual-chapter-6.pdf>.

restrictions increased from 27 percent in 2010 to 47 percent in 2021.²²⁰ This confirms previous research published by MedPAC that found Medicare beneficiaries now face access barriers for nearly half of all medicines covered in Part D.²²¹

Further, changing incentives from the IRA could result in plans choosing to cover medicines very differently; they may impose tighter formularies or stricter utilization management than they have historically, jeopardizing beneficiary access, particularly for conditions where broad formulary access is critical. We note that therapeutically alternative medicines in a given class may not be appropriate for some patients who may need a particular medicine. For example, rheumatoid arthritis patients are more likely to fail on multiple medicines before having a positive clinical response to a given product. If plans narrow access to certain medicines due to dynamics introduced by government price setting, patients who are stable on a given medication may lose access and be forced to switch to an alternative medicines that is not optimal for their unique circumstances, which could result in adverse health outcomes.^{222,223} With changing formulary dynamics caused by government price setting, PhRMA is concerned that formulary restrictions are likely to increase, resulting in significant risk to patients needing innovative medicines to treat difficult to treat conditions such as cancer and autoimmune conditions. Numerous studies have found that switching stable patients to a new medicine for non-clinical reasons leads to poor side effects and increased nonadherence and is often associated with negative health outcomes.²²⁴ Given the potential for significant disruption as a result of the government price setting layered on top of Part D redesign, ***PhRMA recommends that CMS, through rulemaking, create safeguards that limit plan actions to disrupt patients who are stable on therapeutic regimens, including both selected drugs and their competitors.***

PhRMA urges CMS to maintain and protect the current Part D coverage standards for medicines. Part D requires plan formularies to include at least two drugs per class and all or substantially all of the drugs within the six protected classes of concern. We note that at least two drugs per class is a minimum standard which Part D plans can choose to exceed. Part D also requires plans to cover all or substantially all drugs in the six protected classes: immunosuppressants, antidepressants, antipsychotics, anticonvulsants, antiretrovirals, and antineoplastics. PhRMA has long maintained that these formulary protection standards are important to protect Medicare beneficiaries, many of whom have multiple chronic conditions with several medications that could contraindicate each other and who need access to a wider variety of medication options. According to a 2022 analysis by the CBO, per enrollee use of prescription medicines increased in Medicare Part D from an average of 48 prescriptions per year in 2009 to 54 in 2018,²²⁵ a trend that will likely continue. Even without the substantial changes to the Part D program that are going to occur, in many cases, the vulnerable populations covered in Medicare and their health care providers need to have access to a broad range of medications, beyond just two drugs per class.

PhRMA recommends that CMS continue to enforce existing formulary requirements and important non-discrimination controls that ensure patient access to medicines. In the rapidly changing post-IRA environment, it is critical that CMS maintain and strengthen existing Part D beneficiary protections to ensure robust access to medicines. To protect patient access to affordable prescription medicines in Medicare Part D, CMS will need to

²²⁰ Marsh, T. (2021). The Big Pinch: New Findings on Changing Insurance Coverage of Prescription Drugs. GoodRxHealth. Available at: <https://www.medpac.gov/document/july-2022-data-book-health-care-spending-and-the-medicare-program/>.

²²¹ MedPAC. (2022). July 2022 Data Book: Health Care Spending and the Medicare Program. Data Book Chart 10-15, p. 27-28. Available at: <https://www.medpac.gov/document/july-2022-data-book-health-care-spending-and-the-medicare-program/>.

²²² American College of Rheumatology. (2023). American College of Rheumatology Position Statement: Patient Access to Biologics. Available at: <https://www.rheumatology.org/Portals/0/Files/Patient%20Access%20to%20Biologics%20aka%20Model%20Biologics.pdf>.

²²³ Atzeni, Fabiola et al. (2016). Switching rheumatoid arthritis treatments: an update. *Autoimmunity reviews*. 10,7: 397-403. DOI:10.1016/j.autrev.2011.01.001.

²²⁴ Nguyen E, Weeda E, Sobieraj D, et al. (2016). Impact of Non-Medical Switching on Clinical and Economic Outcomes, Resource Utilization and Medication-Taking Behavior: A Systematic Literature Review. *Current Medical Research and Opinion*. 32(7):1281-1290. Available at: <https://pubmed.ncbi.nlm.nih.gov/27033747/>.

²²⁵ CBO Report. (2022). Prescription Drugs: Spending, Use, and Prices. Available at: <https://www.cbo.gov/publication/57772#:~:text=Use%20of%20prescription%20drugs%20among,year%E2%80%942013%20percent%20increase>.

aggressively oversee Part D plan behavior when it comes to bidding, most notably around benefit designs that attempt to manipulate the Part D patient protections to hide discriminatory practices.

Further, CMS must not lose sight of the importance of strong beneficiary protections and appeals in the midst of so many fundamental changes to Part D. To that end ***PhRMA encourages CMS to re-examine and update rules around coverage determinations, appeals, and tiering exceptions*** to allow beneficiaries to appeal for lower cost sharing or exceptions for clinical reasons, to require clear language in Part D plan materials/websites that explains the exceptions process, and to allow medicines on the specialty tier to be subject to the tiering exceptions process. We also call on the Agency to enhance transparency and public reporting of these beneficiary protections and appeals outcomes.

Finally, in addition to rigorously maintaining and overseeing the existing Part D beneficiary protections, CMS should take additional steps to ensure meaningful choice of plans for beneficiaries. PhRMA is concerned that as the government drug “negotiation” program continues its annual process of selecting and setting prices for an increasing number of drugs, these dynamics could result in the rapid standardization of Part D plan formulary designs. Plans will be required to include all selected drugs on formularies and, in time, could also respond with severe access limitations on all competing non-selected drugs. This could lead to fewer meaningfully different options for beneficiaries to choose from when evaluating and selecting a Part D plan that will provide affordable access to their medications. It is imperative that CMS guard against these potential unintended consequences.

VIII. Conclusion

PhRMA appreciates your consideration of these comments. Please feel free to contact Jenny Bryant at jbryant@phrma.org or James Stansel at jstansel@phrma.org if there is any further information we can provide or if you have any questions about our comments.

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Jenny Bryant
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Executive Vice President and General Counsel
PhRMA

Exhibit A – Minimum Part D Data Fields Required for Verification of MFP-eligible Patients

In order to verify patient eligibility for the MFP and the calculation of MFP discount amounts owed by the manufacturer, at a minimum, CMS should ensure that manufacturers have access to the following minimum data fields on a detailed claims-level basis. Furthermore, CMS should also ensure manufacturers choosing to sell to pharmacies at a net price no higher than the MFP also have access to these data fields to improve program integrity. The majority of these data fields are already available through the PDE record, reducing the burden of sharing these fields with manufacturers.

Data Item	PDE Field Name (if Applicable)
Date of Service (i.e. date filled)*	Date of Service
Prescription ID Number*	Prescription Service Reference Number
Part D Contract ID and Part D Plan Benefit Package ID	Plan Contract ID and Plan Benefit Package ID
De-identified Part D Beneficiary ID	Medicare Beneficiary Identifier
Prescriber National Provider Identifier (NPI)	Prescriber ID
Pharmacy NPI*	Service Provider ID
National Drug Code (NDC)*	Product Service ID
Days Supply*	Days Supply
Quantity Dispensed*	Quantity Dispensed
Fill Number*	Fill Number
Paid Date (date the Part D plan paid the pharmacy)	Paid Date
Claim Status (whether the claim was paid or reversed)	
340B and non-340B Indicators (if adopted by CMS)	
340B Clearinghouse Determination (if adopted by CMS)	
340B Ceiling Price (received from Clearinghouse)	
Maximum Fair Price (MFP)	
Pharmacy Acquisition Cost**	
MFP Discount (Acquisition Cost less the MFP)**	

* These fields are already provided to manufacturers as part of the detailed data reports under the CGDP.

** This should be read consistent with PhRMA’s position outlined in section I(f) of this comment letter that CMS should use an alternative metric such as WAC instead of acquisition cost.

Exhibit B – Example of Non-Disclosure Agreement

Attachment 5 Non-Disclosure Agreement

CONTRACTOR EMPLOYEE COMMITMENT TO PROTECT NON-PUBLIC INFORMATION NON-DISCLOSURE AGREEMENT FOR HEALTH AND HUMAN SERVICES/ASPR

I, _____ hereby consent to the terms in this Agreement in consideration of my being granted confidential access to certain United States Government documents or materials containing sensitive but unclassified information.

Access to non-public information may be required in the performance of my official duties, while working under the following contract or sub-contract with the Department of Health and Human Services (HHS), Assistant Secretary for Preparedness and Response (ASPR):

Contract Number _____ between _____ and my employer _____.

To carry out the duties and functions of the United States (U.S), certain information may be disclosed to Contractors that are authorized representatives of the U.S. for the purposes of the disclosure and this Contractor Non-Disclosure Agreement. Such disclosure shall be considered authorized and not a disclosure to the public or outside the Government.

Should I have access to non-public information, I agree that I shall not release, divulge, publish, or disclose such information to unauthorized persons. I shall protect such information and will employ all reasonable efforts to maintain the confidentiality of such information. These efforts shall be no less than the degree of care employed by HHS to preserve and safeguard sensitive information. I will not disclose proprietary information designated "For Official Government Use Only" which has been received in connection with the Health and Human Services Professional Scientific Services contract, except on a need-to-know basis as instructed by the client. Prior to any disclosure to any other Government personnel or any other support contractor personnel, I will verify with the Contracting Officer/Contracting Officer Representative that the individual has signed a non-disclosure agreement with the Contracting Officer/Contracting Officer Representative substantially the same as this agreement. I understand that my obligation not to disclose information applies to information, which I have already received and to information I will receive in the future.

I acknowledge that the unauthorized disclosure of non-public information would violate this agreement; may additionally violate federal law, regulations or policy; and could form the basis for legal action against me or against my employer. I further acknowledge that unauthorized disclosure of said information may compromise the security of the HHS and violate the terms of the aforementioned contract with the United States Government.

I further certify that there are laws and regulations which provide for criminal and/or civil penalties for improper disclosure, including but not limited to:

- 18 U.S.C; 641 (Public Money, Property or Records)
- 18 U.S.C. 1832 (Trade Secrets)
- 18 U.S.C. 1905 (Disclosure of Confidential Information)
- 5 U.S.C.552a (Privacy Act)

April 13, 2023

Deputy Administrator and Director of Center for Medicare
Centers for Medicare & Medicaid Services
Department of Health and Human
Services Room 445-G
Hubert H. Humphrey Building
200 Independence Avenue, S.W.
Washington, D.C. 20201

ELECTRONIC DELIVERY TO IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Initial Guidance

Dear Dr. Seshamani:

The Plasma Protein Therapeutics Association (PPTA) is pleased to have this opportunity to comment on the initial guidance on the Medicare Drug Price Negotiation Program (Initial Guidance) issued by the Centers for Medicare & Medicaid Services (CMS).¹ PPTA is the standard setting and global advocacy organization that represents plasma donation centers and manufacturers of plasma protein therapies. Our U.S. membership includes ADMA, Grifols, Kedrion SpA, and Takeda. PPTA strives to ensure that Medicare beneficiaries continue to have appropriate access to life-saving plasma protein therapies. We are pleased to see CMS continues to recognize the unique nature of plasma and is implementing the IRA statutes in a manner consistent with historical recognition of the fragile plasma-based therapy ecosystem. We believe this minimizes and limits disruption to this ecosystem which is critical to ensuring patients retain access to necessary therapies.

BACKGROUND

Plasma protein therapies are made from human plasma² donated by healthy individuals or by using recombinant technology.³ It is essential that plasma protein therapies have adequate reimbursement due to their unique nature. Manufacturers of plasma-derived therapies depend upon donated plasma from healthy, committed

¹ The initial guidance is available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

² Human plasma is the clear liquid portion of blood that remains after the red blood cells, leukocytes, and platelets are removed. Due to its human origin, complexity, and richness in therapeutically useful proteins, human plasma is a unique biological material. See Thierry Burnouf, *Plasma Proteins: Unique Biopharmaceuticals – Unique Economics*, in 7 PHARMACEUTICALS POLICY AND LAW, BLOOD, PLASMA AND PLASMA PROTEINS: A UNIQUE CONTRIBUTION TO MODERN HEALTHCARE 209 (2005, 2006).

³ Recombinant therapies are only available for clotting factors and C1 esterase inhibitors; plasma-derived therapies are the only life-saving treatment for most plasma protein deficiencies.

individuals as the raw material for therapeutic production. The process for collecting donated plasma is highly regulated, resource-intensive, and time-consuming, with a production process spanning seven to ten months. Individual proteins within plasma are isolated for therapeutic use through distinct fractionation processes. The result is plasma protein therapies that are sole source biologicals that produce different therapeutic outcomes depending on the patient.

Many patients struggle to access providers who have sufficient expertise to treat their conditions, and patients may experience challenges in accessing treatment both geographically and at the appropriate site of care. An analysis of access issues by the Department of Health and Human Services (HHS) Office of the Assistant Secretary for Planning & Evaluation⁴ found that previous changes in Medicare reimbursement policy resulted in access challenges, treatment delays, and shifts in site of service for individuals who use plasma protein therapies. Another study⁵ and a data analysis reached a similar conclusion.⁶ The risks to patient health outcomes underscore the need for a reimbursement framework that ensures access to all therapies.

DISCUSSION

Under the Initial Guidance, CMS will exclude plasma-derived products when identifying qualifying single source drugs as described in section 30.1.3 of this memorandum. Under the Initial Guidance, a plasma-derived product is a licensed biological product that is derived from human whole blood or plasma, as indicated on the approved product labeling, with CMS referring to certain FDA websites to determine if a product is subject to the exclusion. Consistent with section 30.1.3, all plasma protein therapies are rightfully subject to the exclusion. This result is an essential one to ensure continued patient access to these critical therapies, for reasons detailed below, and thus we commend CMS for the exclusion of plasma protein therapies from the Medicare Drug Price Negotiation Program.

Plasma protein therapies, as a class, have a longstanding history of special recognition by federal policymakers in acknowledgement of the non-interchangeability, complex sourcing and production process for plasma medicines. These biological products treat patients who predominantly have rare diseases, and most are orphan drugs. The starting material for plasma derived medicines is human plasma collected from

⁴ HHS, Office of the Assistant Secretary for Planning and Evaluation, *Analysis of Supply, Distribution, Demand, and Access Issues Associated with Immune Globulin Intravenous (IGIV)*, Final Report (February 2007) at pp. 4-31 (ASPE Report).

^{3 5} Tomas Philipson & Anupam B. Jena, *The Impact of Medicare Modernization Act Reimbursement Changes on the Utilization of Intravenous Immune Globulin*, The University of Chicago; The Irving B. Harris Graduate School of Public Policy Studies. This study found that after a reduction in Medicare reimbursement rate for intravenous immune globulin (IVIG) at the start of 2005, the average number of IVIG claims among Medicare eligible individuals grew more slowly than in the non-Medicare eligible population, despite growing at the same rate in the previous three years. There was a significant reduction in the share of IVIG claims for Medicare beneficiaries originating in the physician office with no accompanying change in the non-Medicare population. Changes in the Medicare reimbursement of IVIG negatively impacted access to IVIG.

⁶ The Moran Group, 2003-2010 IVIG [Intravenous Immune Globulin/SCIG [Subcutaneous Immune Globulin] Utilization by PID [Primary Immune Deficient] Patients by Site of Service (Dec. 21, 2012) (noting a significant shift in the site of service of IVIG utilization after implementation of reimbursement cuts as a result of the Medicare Modernization Act).

donors. The amount of source plasma needed to manufacture enough product to treat only one patient annually can exceed 1,300 donations for certain therapies. Furthermore, these products take 7 to 12 months from the time of plasma donation to the delivery of treatment to a patient.

Since 2019, CMS and FDA have had continuing concerns over availability and access to these life-saving therapies and maintaining sufficient collections of plasma. Plasma protein therapies are often subject to various external influences that can affect plasma donation and collection. Plasma protein therapies are, by nature, intrinsically fragile and difficult to fractionate into medicine. The starting material collection process for all plasma protein therapies is influenced greatly by donor concerns like pandemics and man-made problems such as an international border crossing ban. Due to this unique starting material and production process, the cost structure for plasma therapies is significantly different than small molecule pharmaceuticals. For plasma products, the raw materials and manufacturing costs make up 57% of overall costs, compared to 14% for small molecule drugs. During the pandemic and border crossing issues the ingredient costs for plasma derived medicines increased significantly. This variable and very divergent cost structure means that drug price negotiation models are not well suited to this class of products.

Federal policymakers have previously recognized this by exempting this class of therapies from certain Medicare policy proposals, including:

- In 2020, In the Most Favored Nation interim final rule, CMS exempted IVIG from the model based on potential supply impacts⁷;
- In 2005, CMS attempted to implement a third-party vendor model for Medicare Part B drugs, but exempted plasma products because of the importance of maintaining patient access to all products⁸; and
- In 2006, in response to concerns about access to IVIG after implementation of the Medicare Modernization Act, CMS established a temporary pre-administration service payment to compensate providers for services required to locate and acquire adequate product.⁹

The Initial Guidance properly continues the recognition of the importance of plasma protein therapies for hundreds of thousands of patients and the unique nature of the plasma protein therapy industry by excluding these products from the Medicare Drug Price Negotiation Program.

CONCLUSION

We are grateful for this opportunity to offer comments to CMS on the Initial Guidance, focusing specifically on the exclusion of plasma-derived products when identifying qualifying single source drugs. CMS has correctly included plasma protein therapies within this exclusion and that should continue to be the case throughout CMS's

⁷ 85 Fed. Reg. 76180, 76191 (Nov. 27, 2020).

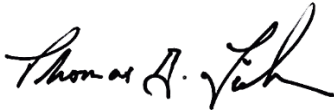
⁸ 70 Fed. Reg. 39022, 39029 (Jul. 6, 2005).

⁹ 70 Fed. Reg. 70116, 70220 (Nov. 21, 2005).

implementation of the Medicare Drug Price Negotiation Program for the reasons discussed above.

Thank you for considering our comments, and please feel free to contact Thomas Lilburn, Senior Director of Government Relations at (443) 458-4682 or tlilburn@pptaglobal.org if you have any questions.

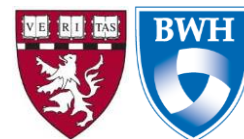
Sincerely,



Thomas Lilburn
Sr. Director of Government Relations



PORTAL
Program On Regulation, Therapeutics, And Law



Division of Pharmacoepidemiology and Pharmacoeconomics
Harvard Medical School and Brigham & Women's Hospital
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April 14, 2023

Via Electronic Submission

Centers for Medicare & Medicaid Services
75000 Security Boulevard
Baltimore, Maryland 21244

RE: Comments on CMS' Medicare Drug Price Negotiation Program Initial Guidance

We are members of the Program On Regulation, Therapeutics, And Law (PORTAL) at Brigham and Women's Hospital and Harvard Medical School. PORTAL is one of the largest, non-pharmaceutical industry-funded academic research centers in the US devoted to investigating drug prescribing, outcomes, and policy. We applaud CMS' initial guidance on the implementation of Medicare price negotiation under the Inflation Reduction Act of 2022. Effective implementation of this policy is vital to ensure that Medicare beneficiaries and taxpayers benefit from fair drug prices. We recently published a study simulating the impact of price negotiation from 2018-2020 and found that, in just the first 3 years of drug price negotiation, Medicare could lower prescription drug spending by 5% by accepting the statutory ceiling price in the law, and even more if negotiations lead to lower prices.¹

In this submission, we provide some specific comments aimed at sharpening and clarifying key pieces of the framework for drug price negotiation. Overall, we are supportive of the approach outlined by CMS. The issues raised here are meant to provide constructive feedback to help strengthen the guidance, minimize the likelihood that brand-name manufacturers avoid fair negotiations, and anticipate effects on the pharmaceutical supply chain.

Sincerely,
Benjamin N. Rome, MD, MPH
Sarah Gabriele, LLM
Hussain Lalani, MD, MPH
Edward Cliff, MBBS, MPH
C. Joseph Ross Daval, JD
William B. Feldman, MD, DPhil, MPH
Ameet Sarpatwari, JD, PhD
Aaron S. Kesselheim, MD, JD, MPH

¹ Rome BN, Nagar S, Egilman AC, et al. Simulated Medicare Drug Price Negotiation Under the Inflation Reduction Act of 2022. *JAMA Health Forum*. 2023;4(1):e225218. doi:[10.1001/jamahealthforum.2022.5218](https://doi.org/10.1001/jamahealthforum.2022.5218).

30.1 Identification of Qualifying Single Source Part D Drugs for Initial Price Applicability Year 2026

CMS plans to treat fixed-dose combinations separately from drugs that contain the same active ingredients / active moieties. While this may be sensible in some cases, it creates an opportunity for drugmakers to avoid negotiation by splitting the market between drugs with a fixed-dose combination alternative. For example, antiretrovirals to treat human immunodeficiency virus (HIV) are frequently marketed as fixed-dose combinations; if drugmakers could co-formulate new molecular entities with a variety of older ones, they could maintain lower Medicare spending on each product to delay being selected for negotiation or, in some cases, prohibit selection by keeping products below the \$200 million Medicare spending threshold necessary to be selected. CMS should instead consider aggregating sales for fixed-dose combinations with other dosage forms containing the newest active ingredient if the products are made by the same company.

By contrast, under the current guidelines, CMS plans to aggregate the sales of active ingredients with different indications and/or routes of delivery, which may be problematic. For example, fluticasone propionate is approved as a nasal spray to treat nonallergic rhinitis (Flonase, NDA 020121) and as an orally inhaled powder to treat asthma (Flovent, NDA 020833). Both products are made by GlaxoSmithKline. Flonase has marketed generic versions that would preclude it from being selected for negotiation, but Flovent does not yet have generic competition. As a result, aggregating sales for these two different products would preclude CMS from negotiating prices for Flovent, which had gross Medicare spending of nearly half a billion dollars in 2021. One potential solution is for CMS to manually review products with different routes of administration before they are aggregated, and to only aggregate such products if the labeled indication(s) are similar.

The guidance also states that bona fide generic or biosimilar competition for “*any strength or dosage form of a potential qualifying single source drug*” would disqualify a drug from being considered for negotiation. This poses a problem, because drug companies frequently engage in product hopping from one formulation to another, actively moving patients to the newer version that often has longer patent protection. If generic or biosimilar competition for the drug’s earliest version precludes negotiation, the newer version of the product should still be eligible for negotiation. We recommend that CMS determine if a given drug would be eligible for negotiation if the strength or dosage forms with generic competition were excluded. For example, if a brand-name drug comes in 2 different formulations and has generic competition for only 1 of these formulations, then the other formulation should still be eligible for price negotiation if its annual gross Medicare spending is above the \$200 million threshold and if the drug has no other reasons for exclusion.

30.1.1 Orphan Drug Exclusion from Qualifying Single Source Drugs

We have concerns about this exclusion. First, we do not see a good reason why drugs treating rare diseases that earn more than \$200 million in Medicare sales should be excluded from negotiation. The fact that drugs qualify based on Medicare sales is a marker that they are commercially successful. It costs less for drug companies to develop orphan-designated drugs than drugs that treat common conditions.²

Second, this exclusion, as implemented, could have unintended consequences for the repurposing of rare disease drugs to treat other rare diseases. For example, pomalidomide (Pomalyst) was initially approved by the FDA in 2013 to treat multiple myeloma, a condition for which the drug was granted an orphan designation in 2003. In 2018, the drug was granted a second orphan designation for the treatment of Kaposi sarcoma, and the

² Wouters OJ, McKee M, Luyten J. Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. *JAMA*. 2020; 323(9):844-853. doi:[10.1001/jama.2020.1166](https://doi.org/10.1001/jama.2020.1166).

drug's label was expanded to include the treatment of AIDS-related Kaposi sarcoma in 2020. Had this second indication not been added to the drug's label, the drug might have qualified for the orphan drug exclusion. This creates a perverse incentive, in which a maker of a commercially successful rare disease drug may choose not to study the drug's effectiveness and safety for other indications.

While CMS cannot remove the sole-orphan exemption from the IRA, there is an important issue that CMS should address in guidance. To be eligible for this exclusion, the guidance specifies that drugs must *“be designated as a drug for only one rare disease or condition under section 526 of the FD&C Act.”* Drug companies frequently seek orphan designations several years before these conditions may be added to the drug's labeling. In cases where a drug is currently approved for a single orphan-designated disease but has one or more additional orphan designations that are not yet FDA-approved, drugmakers may seek to withdraw the designated indication if doing so would allow them to qualify for the orphan drug exclusion. We would suggest that CMS clarify how such withdrawn designations will be handled regarding this exclusion. We recommend that such withdrawals should not exempt manufacturers from drug price negotiation.

30.1.3 Plasma-Derived Product Exclusion from Qualifying Single Source Drugs

We also have concerns about the exclusion of plasma-derived products. First, we do not see a good reason why otherwise eligible plasma-derived products should be excluded from negotiation: there were at least 5 such products with Medicare spending over \$200 million in 2021, all of which are immunoglobulins. Rather, the fact that prices remain high despite the availability of multiple therapeutically similar immunoglobulin products suggests that this is a product class that could benefit from Medicare price negotiation. Further, highly expensive plasma-derived products such as factor replacement therapy pose major affordability and access problems for many patients.

We recognize that CMS cannot amend the IRA to include plasma-derived products. However, we believe that CMS could better clarify which products will be considered plasma-derived. The statute defines a plasma-derived product as “a biological product that is derived from human whole blood or plasma.” CMS should clarify whether, for example, cellular and gene therapies that may be derived using apheresis from a patient's blood would therefore be entirely excluded from negotiation. We do not believe that such products should be excluded and would recommend that CMS explicitly identify such products in its final guidance as eligible for drug price negotiation.

The initial CMS guidance states that CMS will identify plasma-derived products from the following FDA website: <https://www.fda.gov/vaccines-blood-biologics/blood-blood-products/approved-blood-products>. This page includes a list of fractionated plasma products but also includes a list of all biologic products regulated by the FDA Center for Biologics Evaluation and Research, which includes a wide range of products, not all of which are likely to meet the definition of plasma-derived products. We recommend that CMS clarify the definition so that only fractionated plasma products (and not those listed on the “Licensed Biological Products with Supporting Documents” page) will be excluded from negotiation. These products are listed here: <https://www.fda.gov/vaccines-blood-biologics/approved-blood-products/fractionated-plasma-products>.

40.2.1 Confidentiality of Proprietary Information

“CMS is seeking comment about the proper balance between the public's interests in transparency and the protection of business information in this context.”

We urge CMS to be very selective about which data elements it treats as confidential proprietary information. The status quo is that prescription drug prices are shrouded in secrecy; there have been several efforts in recent years to make prices more transparent for consumers, including via state transparency laws.^{3,4} Drug manufacturers, insurers, and pharmacy benefit managers have all fought to maintain the secrecy of discounts and prices through the supply chain. However, the resulting information asymmetry harms patients who are partially or fully exposed to the full pre-discount price based on their health insurance status or benefit design. It also impedes manufacturer competition and limits accountability on whether rebates are being translated into savings for insurers and patients. Transparency is a core element of competitive markets.

While CMS may have reasons to treat some data elements as proprietary during this first round of negotiation, we recommend that the guidance clarify that CMS reserves the right to re-classify elements as non-proprietary in subsequent years. For example, while individual net prices negotiated between the manufacturer and each Part D plan may be confidential, the weighted average net price across all Part D plans may not be subject to the same restraints. Average net prices for selected drugs have been published in staff reports released as part of an investigation by the US House Committee on Oversight and Accountability.⁵ Similar arguments could be used to improve transparency of Medicaid best prices, 340B discounts, and federal supply schedule and Big 4 prices.

In addition, given substantial public interest, we would recommend that CMS include as many details as possible about the negotiation process that helps patients understand how CMS arrived at the maximum fair price, including data used to derive the initial offer, the amount of the initial offer, amount of the manufacturer's counteroffer, and any new information that informed a change between the initial offer and the final MFP.

50.2 Evidence about Therapeutic Alternatives for the Selected Drug

“CMS is soliciting comment on other metrics, in addition to QALYs, that may treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill and that CMS should also exclude from consideration when developing offers and reviewing counteroffers.”

We believe that CMS should consider both life extension and improved quality of life when measuring the comparative effectiveness of a selected drug and therapeutic alternatives. In many cases, drugs do not extend life, such as symptomatic treatments for arthritis. In these cases, the use of QALYs or other measures that assess quality of life is non-discriminatory. In cases where drugs do extend life, CMS should consider alternative measures that incorporate quality of life but treat extended life equally for all individuals. One example of such a measure is the equal value life year gained (evLYG). The use of such measures would be helpful for CMS in determining a maximum fair price, and we believe they align with the statutory requirements.

³ Feldman WB, Rome BN, Avorn J, Kesselheim AS. The Future of Drug-Pricing Transparency. *New Eng J Med* 2021; 384:489-491. doi: [10.1056/NEJMp2033734](https://doi.org/10.1056/NEJMp2033734).

⁴ 2023 State Legislative Action to Lower Pharmaceutical Costs. National Academy for State Health Policy. Updated March 31, 2023. <https://nashp.org/2023-state-legislative-action-to-lower-pharmaceutical-costs/>

⁵ Chairwoman Maloney Releases Comprehensive Staff Report Culminating the Committee's Sweeping Drug Pricing Investigation. US House Committee on Oversight and Accountability. Published December 10, 2021. <https://oversightdemocrats.house.gov/news/press-releases/chairwoman-maloney-releases-comprehensive-staff-report-culminating-the-committee>

60.1 Establishment of a Single Proposed MFP for Negotiation Purposes

The choice by CMS to negotiate prices for a 30-day equivalent supply rather than per unit is sensible for many drugs used to treat chronic conditions. However, in some cases, 30 days may not be the optimal time frame by which to evaluate drugs. For example, some drugs are administered once (e.g., a 1-time gene therapy) or used for a short, fixed period to treat an acute condition (e.g., an antibiotic or antiviral). For this reason, CMS may wish to allow for flexibility in selecting an alternative supply of the drug if it is not used chronically.

This same concern applies when comparing the price of the selected drug to the prices of therapeutic alternatives. If the therapeutic alternatives have a different dosing schedule than the selected drug, comparing prices per 30-day supply may not be sensible. For example, denosumab is an injection given every 6 months for treating osteoporosis; therapeutic alternatives may include oral bisphosphonates (often dosed once a week) and injected bisphosphonates (dosed once a year). Comparing prices per 30-day supply, in this case, may not adequately capture variations in the price of treatment, and CMS should consider using the annual cost of treatment instead.

60.3.2 Developing a Starting Point for the Initial Offer

“If there are multiple therapeutic alternatives, CMS intends to consider the range of net prices and/or ASPs as well as the utilization of each therapeutic alternative to determine the starting point within that range.”

For selected drugs with multiple therapeutic alternatives, we would recommend that the lowest net price for a therapeutic alternative serve as the starting point for the initial offer. Such an approach would ensure that any amount that CMS pays in excess of the lowest-cost alternative is justified by the drug’s comparative safety and effectiveness.

“If the selected drug has no therapeutic alternative, if the price of the therapeutic alternatives identified is above the statutory ceiling for the MFP (described in section 60.2 of this memorandum), or if there is a single therapeutic alternative with a price above the statutory ceiling, then CMS intends to determine the starting point for the initial offer based on the Federal Supply Schedule (FSS) or “Big Four Agency” price (“Big Four price”).”

In case when a selected drug has no pharmacologic therapeutic alternatives, we would recommend CMS consider using prices negotiated by other countries as a starting point for the initial offer, especially if foreign prices are lower than the FSS or Big Four price. Nearly every other large, industrialized country has a process for evaluating evidence and negotiating prices when drugs are first approved. CMS should leverage these existing assessments to determine a maximum fair price.

60.6.1 Explanation for the MFP

“Section 1195(a)(2) of the Act requires CMS to publish an explanation for the MFP no later than March 1 of the year prior to the initial price applicability year, which will be March 1, 2025 for initial price applicability year 2026.”

We would encourage CMS to publish the explanations for the published MFPs before the statutory deadline, ideally alongside the published MFPs, which must be published by September 1, 2024, for the first 10 negotiated drugs. Transparency around these explanations will provide essential information for a variety of

stakeholders, including state governments and private payers that may wish to use this information as part of their own drug price negotiation processes.

90.4 Monitoring for Bona Fide Marketing of Generic or Biosimilar Products

“CMS is seeking comment on the most effective ways to monitor whether robust and meaningful competition exists in the market after a selected drug ceases to be a selected drug.”

The CMS guidance states that drugs will be excluded from negotiation once they have bona fide generic or biosimilar competition. CMS has identified several tools that it may use to monitor for bona fide competition, including assessing whether the generic drug or biosimilar is consistently available for purchase by wholesalers and whether patients can access generic and biosimilar versions in pharmacies and clinics. CMS also plans to analyze the share of generic or biosimilar uptake based on Medicare claims data. We think that each of these approaches is important, though determining the minimum thresholds required for bona fide generic competition will be challenging.

One type of generic or biosimilar competition that, in our opinion, should not count as bona fide competition, regardless of market share, is entry based on “limited-supply agreements.” These agreements occur when a brand-name manufacturer agrees to allow for generic or biosimilar competition (usually in exchange for dropping litigation) and the generic or biosimilar firms agree to release their products in a limited fashion according to agreed-upon terms. Brand-name manufacturers may have a strong financial incentive to avoid Medicare negotiation, and a possible strategy to do so may be via limited-supply agreements with generic or biosimilar firms. For example, a brand-name company may allow a generic firm to obtain 20% market share in the US (leaving 80% for the brand-name firm) for a period so that its drug is excluded from Medicare negotiation during that time.

While the nature of legal settlements between brand-name and generic firms is often shrouded in secrecy, we know that limited-supply agreements already occur in the pharmaceutical industry. In our review of Hatch-Waxman patent challenges from 2003 to 2022 (also known as “paragraph IV certifications”), for example, we uncovered limited-supply agreements for at least 4 high-cost brand-name products: Lamictal⁶ (lamotrigine), Solodyn⁷ (minocycline), ProAir HFA^{8,9} (albuterol), and Revlimid^{10,11} (lenalidomide). In the case of ProAir HFA, the brand-name firm Teva agreed to settle litigation with Perrigo in June 2014 and allow the limited release of generic albuterol inhalers from December 2016 to June 2018, at which point limits would no longer apply. In this case, Perrigo’s generic product did not end up receiving FDA approval until 2020. Bristol Myers Squibb entered into agreements with at least two generic firms (Dr. Reddy and Sun Pharma) to allow limited-

⁶ Fields K. Direct Purchasers of Lamictal Certified as a Class in Pay-for-Delay Case. Faruqi & Faruqi, LLP. Published December 17, 2018. <https://www.faruqilaw.com/blog/292/direct-purchasers-of-lamictal-certified-as-a-class-in-pay-for-delay-case>

⁷ Complaint filed by Rite Aid Corporation and Rite Aid Hdqtrs. Corp. against Medicis Pharmaceutical Corp., in Case 1:15-cv-00673-YK, filed on April 6, 2015, available at <http://business.cch.com/ald/RiteAidMedicisComplaint.pdf>

⁸ Palmer E. Teva Reaches Settlement in ProAir[®] HFA Patent Case. *Fierce Pharma*. <https://www.fiercepharma.com/pharma/teva-reaches-settlement-proair%C2%AE-hfa-patent-case>. Published June 20, 2014.

⁹ Teva Reaches Settlement in ProAir[®] HFA Patent Case. Teva Pharmaceutical Industries Ltd. Published June 20, 2014. <https://www.tevapharm.com/news-and-media/latest-news/teva-reaches-settlement-in-proair-hfa-patent-case/>

¹⁰ Sagonowsky E. After win at patent office, Bristol Myers inks Revlimid deal with Dr. Reddy’s. *Fierce Pharma*. <https://www.fiercepharma.com/pharma/after-patent-win-at-pto-bms-inks-revlimid-settlement-dr-reddy-s>. Published September 17, 2020.

¹¹ Kansteiner F. Bristol Myers inks another Revlimid patent settlement—this time with Sun Pharma—as copycats near. *Fierce Pharma*. <https://www.fiercepharma.com/manufacturing/bristol-myers-settles-sun-pharma-for-limited-revlimid-generic-launch-2022>. Published June 22, 2021.

supply sales for generic lenalidomide beginning in 2026. Such agreements may be more pervasive than is publicly known. Generic entry according to limited-supply agreements should not, in our view, count as bona fide generic competition. Rather, IRA negotiation should include brand-name drugs and biologics with limited-supply agreements so long as these drugs and biologics would otherwise qualify.

April 14, 2023

Meena Seshamani, M.D., Ph.D.,

CMS Deputy Administrator and Director of the Center for Medicare
DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Re: Medicare Drug Price Negotiation Program Initial Guidance

Submitted electronically via IRAREbateandNegotiation@cms.hhs.gov

Dear Deputy Administrator Seshamani,

Pursuant to the Centers March 15, 2023, memo addressed to interested parties on the subject of Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments, the LGBTQIA+ Primary Care Alliance (Primary Care Alliance or PCA) submits these comments. The Primary Care Alliance supports the balance of the Centers for Medicare and Medicaid Services (CMS) implementation plan, however, as interested party with a complex relationship to the price of pharmaceutical products, the PCA submits the following comments and recommendations to safeguard the nation's safety net clinics and primary care providers to underserved populations.

Interest and Expertise of the Primary Care Alliance

The Primary Care Alliance includes FQHCs, State Primary Care Associations, community health centers, and other health care organizations and providers throughout the nation, who promote best practices for providing culturally responsive and compassionate health care and related services for persons identifying as lesbian, gay, bisexual, transgender, and gender diverse, queer, intersex, and/or asexual or on the ace spectrum (LGBTQIA+). The Alliance members joining in these comments collectively serve several hundred thousand individuals and families every year, in the Northeast, Mid-Atlantic, Midwest, South, and West. Our members also advocate for federal, state, and local laws and public policies that advance the health and well-being of sexual and gender diverse people, with particular emphasis on persons of color, immigrants, people

with disabilities and chronic illnesses, low-income individuals and families, transgender and gender diverse persons, sex workers, drug users, and other particularly marginalized communities.

Comments of the LGBTQIA+ Primary Care Alliance

CMS SHOULD ENSURE THAT DRUG PRICE NEGOTIATIONS DO NOT UNDERMINE RESOURCES FOR SAFETY NET CLINICS TO PERFORM OUR ESSENTIAL FUNCTIONS

It is our primary concern that we communicate to CMS that actions taken to address the high cost of drugs do not inadvertently decimate the safety net providers that are the cornerstone of the cross-government approach to address health equities for underserved communities of people, including LGBTQ+ people, people living with or at risk for HIV, and Black, Latine, and Asian American and Native American people. As community health centers dedicated to addressing the health and wellbeing of underserved populations, many members of the PCA are participants in the 340B program. The 340B program creates a complex relationship between our health centers and the high price of drugs by funding many of the wrap around services that our most vulnerable patients rely on to access life-saving care. Patient navigation, adherence, retention, and outreach services are all routinely paid for using 340B program revenue. While we support drug price negotiations, CMS should take due care that drug price negotiations do not weaken the health care safety net.

CMS can do so through a number of mechanisms to strengthen the drug price negotiation plan:

1. The Secretary should have the authority to adjust the drug price negotiation plan to ensure the continued vitality of the safety net of community health care centers, federally qualified health centers and look-alikes, and Ryan White program clinics.
2. As Congress has decided that CMS is not allowed to negotiate on drugs for a single rare disease, CMS should encourage more research into medications to treat rare diseases, so that the list of drugs that Medicare can negotiate on can expand.
3. CMS should ensure that randomized controlled trials are not the only types of evidence that are considered in establishing effectiveness of medications and deciding which medications to prioritize for lower prices and therefore greater access (beyond the legally mandated requirements about cost thresholds). Where clinical equipoise does not exist,

evidence from a variety of research designs, including pragmatic trials and non-RCT designs, should be given appropriate weight.

4. While the 6 protected classes of drugs (antidepressants, antipsychotics, anticonvulsants, immunosuppressants, antiretrovirals, and antineoplastics) that Part D has to cover will depress CMS's bargaining power with the manufacturers, weakening the protected classes—as CMMI proposed to do in early 2021—is unacceptable. The protected classes of drugs are essential to protect the health and wellbeing of our patients.
5. CMS should institute robust enforcement mechanisms for manufacturers that attempt to evade or violate the negotiated prices. Spot checks are insufficient and routine. systematic enforcement mechanisms are essential.

Conclusion

The LGBTQIA+ Primary Care Alliance appreciates this opportunity to furnish information to CMS regarding the implementation of the drug price negotiation initial guidance. We continue to appreciate CMS' partnership with our members in advancing the health and wellbeing of the American people. For more information about any subjects mentioned here, please contact Benjamin Brooks, (bbrooks@whitman-walker.org).

Signed,

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CEO/President
Transhealth
Co-Chair of the Primary Care Alliance
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Respectfully submitted, April 14, 2023

Timothy Wang, MPH
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CMS Deputy Administrator and Director of the Center for Medicare

Transmitted via IRAREbateandNegotiation@cms.hhs.gov

April 14, 2023

Joint Comments Regarding Medicare Drug Price Negotiation Guidance

Dear Dr. Seshamani,

Thank you for the opportunity to provide stakeholder feedback as CMS works to enact the new drug price negotiation and inflationary rebate systems established through the Inflation Reduction Act.

Our groups, representing patients, consumers, health care providers and public health experts are committed to ensuring access to affordable medicines and eager to support successful implementation of the law. Many of us have invested years working towards passing laws including these policies, and appreciate that CMS is committed to implementing the objectives of lowering prescription drug prices and reducing costs for millions of older adults and people with disabilities.

We are filing these comments today to register our serious concerns with CMS' proposed approach for developing its negotiated price offer starting point. We strongly urge CMS not to move forward with this approach and to consider other proposed options.¹

Section 60.3 outlines the proposed methodology from CMS for developing an initial price offer in drug price negotiations. CMS proposes in section 60.3.2 to take as a starting point for developing its initial negotiated price offer the average prices available for therapeutic alternatives for the selected drug.

Below, we articulate two major concerns with this approach.

1. Starting with the prices of therapeutic alternatives will lead to ongoing inappropriately high prices.

Evidence shows that drug prices paid under Medicare Part D are significantly higher than those paid under other health programs in the United States, including Medicaid and the Department of Veterans Affairs, as well as those paid in other wealthy countries.^{2,3,4}

¹ Some of the undersigned groups have proposed to use health technology assessments to arrive at a starting point for determining initial price offers in negotiations, while others propose to take a holistic approach to the factors provided in Section 1194(e) of the Act to determine a price based on the cost of innovation and promoting therapeutic advancements. These proposals are clarified further in individual comments provided to CMS from Families USA, Public Citizen, and others.

² Government Accountability Office, *Prescription Drugs: Department of Veterans Affairs Paid About Half as Much as Medicare Part D for Selected Drugs in 2017*, GAO-21-111, January 14, 2021.

³ Mulcahy AW, C.; Tebeka, M.; Schwam, D.; Edenfield, N.; Becerra-Ornelas, A. International Prescription Drug Price Comparisons. 2021; https://www.rand.org/content/dam/rand/pubs/research_reports/RR2900/RR2956/RAND_RR2956.pdf. Accessed April 7, 2023.

⁴ Government Accountability Office, *Prescription Drugs: U.S. Prices for Selected Brand Drugs Were Higher on Average than Prices in Australia, Canada, and France*, GAO-21-282, April 28, 2021.

Current inappropriately high prices, which burden Medicare beneficiaries and taxpayers, are the underlying reason that Congress passed and President Biden signed a law to empower Medicare to negotiate in the first place.

These prices are set by drug corporations under monopoly conditions to maximize profits, while plans face broad coverage obligations under Medicare Part D. Taking prices of therapeutic alternatives set under these conditions as the starting point for developing negotiated price offers would in turn bias the system towards inappropriate high, unfair prices.

2. Starting with the prices of therapeutic alternatives would be a missed opportunity for the law to provide virtuous systemic impact.

In support of its negotiated price offer starting point proposal, CMS argues that “[the prices of therapeutic alternatives] is an important factor when considering the overall benefit that the treatment brings to Medicare beneficiaries.” We agree that pricing of a medicine and its therapeutic alternatives impact Medicare beneficiaries, but we do not believe it follows that prices of therapeutic alternatives should dictate the starting point of prices CMS negotiates.

Rather than provide virtuous systemic impact, the current process CMS is considering would reduce incentives for manufacturers of therapeutic alternatives to lower their prices. Using existing drug prices that have not been negotiated by CMS as the basis for negotiations risks building inertia for higher prices into the system. By instead negotiating a maximum fair price through alternate methods, articulated by some of our organizations in individual comments, CMS’ negotiation process could help reduce the prices of the alternative therapies, since the manufacturers of the alternatives may try to compete on price with that of the negotiated product.

Thank you again for your time and attention. The decisions CMS faces now have the potential to impact pricing and access to medicines for millions of people for years to come. Please reconsider your approach to developing a starting point in negotiations to help ensure Medicare beneficiaries and taxpayers do not continue to pay inappropriately high drug prices.

Sincerely,

Public Citizen
ACA Consumer Advocacy
Arkansas Community Organizations
Center for Medicare Advocacy
Culinary Health Fund
Doctors for America
Georgians for a Healthy Future
Health Care Voices
Knowledge Ecology International
Medicare Rights Center

Families USA
MomsRising
Rights & Democracy
Salud y Farmacos
Social Security Works
T1International USA
U.S. PIRG (Public Interest Research Group)
United States of Care
Unity Fellowship of Christ Church-NYC
VOCAL-NY

April 14, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

RA Capital Management, LP and Orbimed Advisors appreciate the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

RA Capital is a multi-stage investment manager dedicated to evidence-based investing in public and private healthcare and life science companies. The flexibility of its strategy allows RA Capital to provide seed funding to startups and to lead private, IPO, and follow-on financings for its portfolio companies, both facilitating the crossover process and allowing management teams to drive value creation from inception through commercialization.

OrbiMed is a leading healthcare investment firm, with over \$17 billion in assets under management. OrbiMed invests globally across the healthcare industry, from start-ups to large multinational corporations, through a range of private equity funds, public equity funds, and royalty/credit funds. OrbiMed seeks to be a capital provider of choice, providing tailored financing solutions and extensive global team resources to help build world-class healthcare companies.

The IRA puts CMS in a leadership position to define the societal value of medicines, which will shape biomedical investing for decades to come. While only 9 years of market-based pricing for NDA-path drugs is already shifting investment towards BLA drugs, we believe that the proposals below would help investors ascribe some value to NDA-path medicines beyond 9 years (albeit less than in a pre-IRA world). Anything CMS can do to blunt the degree of revenue reduction for drugs it recognizes as “worthy” (taking all relevant parameters of value into account) would hopefully lead to better health outcomes and continued innovation by preserving the investability of NDA-path drugs for people on Medicare that investors believe would meet the value criteria you lay out (which is why it’s also important that those value criteria be clearly defined and

transparently and predictably applied). Our proposals are consistent with CMS's goals of improving health outcomes and promoting value-based, person-centered care.

1) Defining therapeutic alternatives - consider a broad value framework when considering your initial offer

When considering therapeutic alternatives to and clinical benefits of a selected drug, we would encourage you to consider all aspects of a drug's profile that may lead to an improved experience for the person being treated, alleviate caregiver burden, and otherwise contribute to societal value. The societal value of a drug can be better described and quantified using a [Generalized Cost Effectiveness Analysis](#) (GCEA)¹. Given the limitations on using the QALY, we would expect that any cost-effectiveness analysis would likely end up accounting for benefit using equal value life years gained (evLYG). **We would propose that you base your initial offer for each selected drug on a GCEA, not a conventional CEA that ignores many of the demonstrably real elements of value.** If the GCEA estimate for the drug is below the maximum fair price ceiling, you can use the GCEA estimate as the basis for your initial offer. If a drug is above the maximum fair price ceiling, you can simply use the ceiling.

A GCEA analysis accounts for key aspects of a drug's profile valued by the people who need it, their caregivers, and even healthy non-caregivers who derive peace-of-mind from knowing that medicines are there for them in case they might need them. ***This last value, to healthy people, is especially important*** yet entirely overlooked by conventional math, but we know it's real.

Consider, for example, how society spends money on smallpox countermeasures even though no one has smallpox, or how society wants new antibiotics and urges policy like the PASTEUR Act even though there are very few cases of pan-drug resistant infections. Some cancers are now less scary for all of us because we know there is screening technology and medicines that can manage or cure them. HIV is less scary for the whole population because we have effective antivirals. Vaccines restore peace of mind and, in the case of COVID-19, trillions of dollars of economic activity. Although models would have suggested that most people would not have died of COVID-19, what mattered was that billions of people were worried that it might happen to them or their loved ones, so they paid a high price (isolation) to avoid that outcome. Parents of a child with food allergies (and the child themselves) derive peace-of-mind (a measurable

¹ Economists refer to a [value flower](#), whose petals represent the many ways drugs have societal value beyond just the obvious benefit to the people who take them, [and repeatedly have urged that CEAs assessing the societal value of medicines take them into account](#). Economists have [devised a more generalized CEA methodology called GRACE](#) that accounts for [disease severity](#) (most simply, the value to averting death is worth a lot more than 10x the value of improving one's quality of life by 10%) and [insurance value](#) (the value healthy people derive from knowing that a drug is there in case they need it, as with a fire extinguisher). Economists also point out that guidelines urge that CEAs should account for a drug going generic, but the [vast majority of published CEAs ignore this](#) and therefore [undervalue medicines](#). The combination of GRACE and genericization leads to a more generalized framework for appreciating a drug's societal value, which is the basis for many ongoing GCEAs. Economists have given the example of how [drugs for multiple sclerosis](#) and [vaccines](#) have broader societal value than captured by conventional CEA and urge a more comprehensive approach. It's possible for a company to commission a GCEA study that incorporates some of the petals of the flower, such as this [assessment of the checkpoint inhibitor Opdivo for the treatment of 2nd line NSCLC](#). More such studies are on the way.

benefit, whether one uses the QALY or evLYG) from knowing their child carries an epinephrine product even if their child might never actually experience an anaphylactic event. Conventional CEA would require that child to experience anaphylaxis for the epinephrine to have value (akin to requiring a house to catch on fire for a fire extinguisher to have value) whereas GCEA would account for the risk reduction that medicines (and fire extinguishers) offer to everyone, every day, just by existing.

GCEA goes beyond safety and efficacy to include other aspects such as ease-of-use, accessibility for vulnerable populations, and safety and efficacy in specific populations that may be contra-indicated to other drugs. For example, Eliquis and Warfarin are both anticoagulants, but Eliquis has been shown to have a reduced risk of major bleeds, does not require complex monitoring, and has fewer interactions with food and other drugs. As such, people can more easily adhere to therapy with Eliquis and it is accessible even to people in rural areas who cannot easily get to clinics for monitoring. A GCEA would take all this into account and credit Eliquis with its superiority to Warfarin.

The superiority of one medicine compared to others should also be considered in the context of the *future* value of that medicine. Conventional CEA only looks at people that start treatment when the medicine is first approved and assumes that the medicine's price will never change. That ignores that a novel medicine leaves us with forever-improved healthcare. Because we have statins, we never have to worry that cardiovascular disease will ever be as poorly managed as it was before those products came to market. Even now that statins are generic, there are millions of people who are able to access statins at lower prices, reducing their risk of heart attacks and strokes. Conventional CEA ignores all the QALYs or evLYGs generated in future years. It would be as if we considered the merits of investing in clean energy only in terms of what it could do for us today instead of looking out to the future. And yet, the disease burden looming ahead is no less real than the burden of climate change.

There will be those who say that a GCEA is imprecise. And that's true. All CEAs are imprecise. Our concern is that a CEA magnifies that imprecision by assigning demonstrably incorrect values (i.e., zero) to caregiver benefits, risk reduction for currently healthy people, and the magnitude by which a drug's price will drop in the future (worth noting that if there were any doubt before how low its price would go after loss of exclusivity, after the IRA CMS should have no doubts and therefore it would be illogical to model the value of a medicine as if it will never become inexpensive). A GCEA by contrast seeks to ground its valuation in more rather than fewer indices and thereby increases the precision and reliability of the resulting assessment.

2) Transparency - make all documents related to the offer and counter-offer process public

We believe the public, industry, and investors would benefit from having **all offer and counter-offer documents made public**. Consider how the FDA's publication of correspondence for all approved drugs helps maintain public trust in the approval process as well guide drug

developers and investors towards clinical trial designs and drug profiles more likely to result in approvable products.

Drug developers and investors will now be looking to CMS to understand what NDA-path products remain investable, as well as what data they should generate to show value. Ultimately, CMS is accountable to the American people for setting a value framework that will determine which types of drugs for elderly populations get developed over the coming decades. An understanding of this framework will require much more than the high-level explanation provided for the MFP. Industry participants will need to analyze the specific context in which the factors were considered and how CMS responded to company arguments.

We understand your concerns about confidential information. Of the information that companies are submitting to CMS, we view the only sensitive information as R&D costs, unit costs of production, and certain net pricing information. Such information could easily be redacted from the publicly available documents, just as confidential information is currently redacted from FOIA requests and FDA review documents.

We would also like to point out what others have, which is that biomedical R&D relies on a portfolio of investments of which only a few projects turn into commercial products. So a drug's price is not linked to the cost of its own development. The relationship between drug prices and R&D investment goes in the other direction. The higher the rewards investors see today's new medicines earning, the more willing they are to invest more in trying to develop more such medicines that could also justify comparable rewards. The lower the rewards today's drugs generate, whether because their launch prices are lower or their period of profitability has been truncated by the IRA, the less they are willing to invest in more such projects. Ideally, CMS would not place emphasis on or even use whatever information companies provide about a drug's R&D costs.

3) Define a Qualified Single Source Drug by its NDA or BLA to encourage development of new and meaningfully better formulations

Consider a small biotech developing a pill for a chronic condition that affects mainly people on Medicare. The first version of their pill must be taken twice a day with food. The company is also developing a second-generation version of their pill, using the same active moiety as the first version, that only needs to be taken once a day and can be taken without food. This second-gen version is several years behind the first. Before the IRA, investors would encourage the company to develop both versions, expecting that they would be rewarded for the second-gen version since people who take the drug, their caregivers, and their doctors would value its benefits. Today, investors have a quandary. If the negotiation clock starts at 9 years and will be applied to both versions of the pill, will investors be rewarded for investing in the second version? Conversely, should they pause development of the first-gen version, expected to get to market sooner, to save their 9 years for the second-gen version?

We would propose each NDA triggers a new clock to encourage innovation in next-gen versions (and avoid incentives to slow the development of first-gen versions), even if the active moiety is the same. If a new formulation of an active moiety is not valued by the market, doctors can simply not prescribe it and plans can use prior authorization to require that people try the less expensive, price-negotiated version first. But to the extent that the new formulation really is better than the first, then it should be allowed to have its own 9-year period in which to realize the incentive for such superiority (and if a GCEA confirmed that this superiority is cost-effective it might then prompt CMS to impose only the minimum required discount after 9 years).

Another benefit to defining a qualified single source drug by its NDA or BLA is that it would encourage the development of improved versions of existing drugs for orphan indications. RA Capital Management is an investor in Aerovate Therapeutics, which is developing an inhaled version of imatinib for people with pulmonary arterial hypertension (PAH). Oral imatinib showed efficacy in PAH but was not well-tolerated. In fact, those side effects were so severe at effective doses that oral generic imatinib, though inexpensive, is not used for the treatment of PAH. That's why there's an unmet need for a better way of delivering imatinib; Aerovate's inhaled version of imatinib is intended to focus the drug on the lung, thus limiting the side effects related to the drug reaching other parts of the body. Since PAH is an orphan disease, Aerovate's drug should be exempt from negotiations, if approved. However, imatinib itself received multiple orphan drug designations. Does that mean Aerovate will be ineligible for the orphan drug exemption because an irrelevant oral formulation was developed for other diseases? Oral imatinib's orphan drug designations (granted many years ago, to another company, in oncology indications) should have no bearing on Aerovate's eligibility for the orphan drug exemption.

For the purpose of determining eligibility for the orphan drug exemption, CMS should look at only the number of orphan drug designations for the NDA in question vs. looking through across all active moieties.

Certainly, if another version of that moiety could not be used and is not used in place of the formulation in question, then CMS should not lump those formulations together when considering whether the orphan exemption applies.

4) The orphan drug exemption should only count active orphan drug designations for approved indications

Companies often pursue multiple orphan drug designations (ODD) while their drugs are in development. For example, several drugs targeting KRAS G12C-mutated cancers have orphan drug designation in both G12C-mutant non-small-cell lung cancer and colorectal cancer. However, such drugs are only approved in non-small-cell lung cancer. Should such drugs be considered "multi-orphan" since they have ODDs in colorectal cancer, despite not being approved for that indication (yet)? We would recommend clarifying that, for the purposes of counting the number of orphan drug designations to determine single orphan eligibility, CMS will only look to the number of ODDs for approved indications. At a minimum, CMS should not

consider withdrawn ODD applications for the purpose of determining eligibility for the single orphan exemption.

We encourage CMS also to consider only those ODDs for which indications have been approved. Those ODDs for indications that the drug ultimately wasn't approved for only serve to provide R&D tax credits that helped defray the cost of exploring those indications. If vestigial ODDs ended up invalidating ODD-based orphan exemption for the one orphan indication a drug ultimately got approved for, then companies would not file for an ODD until they knew which one indication they would launch their drug for. That would disqualify them from the R&D tax credits for that drug and therefore drive up the cost of orphan drug development. CMS could readily address this concern by adopting a policy of evaluating a drug's eligibility for the orphan drug exclusion based only on those designations with approved indications.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact Chris Morrison by e-mail at cmorrison@racap.com if you have any questions regarding our comments.

Sincerely,

Tess Cameron
Principal
RA Capital Management

Peter Thompson
General Partner
Orbimed Advisors



April 13, 2023

VIA ELECTRONIC DELIVERY to IRAREbateandNegotiation@cms.gov

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244-1850

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Brooks-LaSure:

The Rare Access Action Project, (RAAP) appreciates this opportunity to comment on the initial guidance regarding the Drug Price Negotiation Program (Negotiation Program) under the Inflation Reduction Act of 2022 (IRA) issued by the Centers for Medicare & Medicaid Services (CMS or Agency) on March 15, 2023 (Initial Guidance).¹

RAAP is a registered 501(c)(4) non-profit organization that is a coalition of life sciences and patient stakeholders that explore creative policy solutions to address structural issues in access and coverage. Our priorities are twofold. First, we advocate for policies that stimulate the development of therapies that treat rare diseases. Second, we advance initiatives that ensure rare disease patients have access to the care and treatments they need.

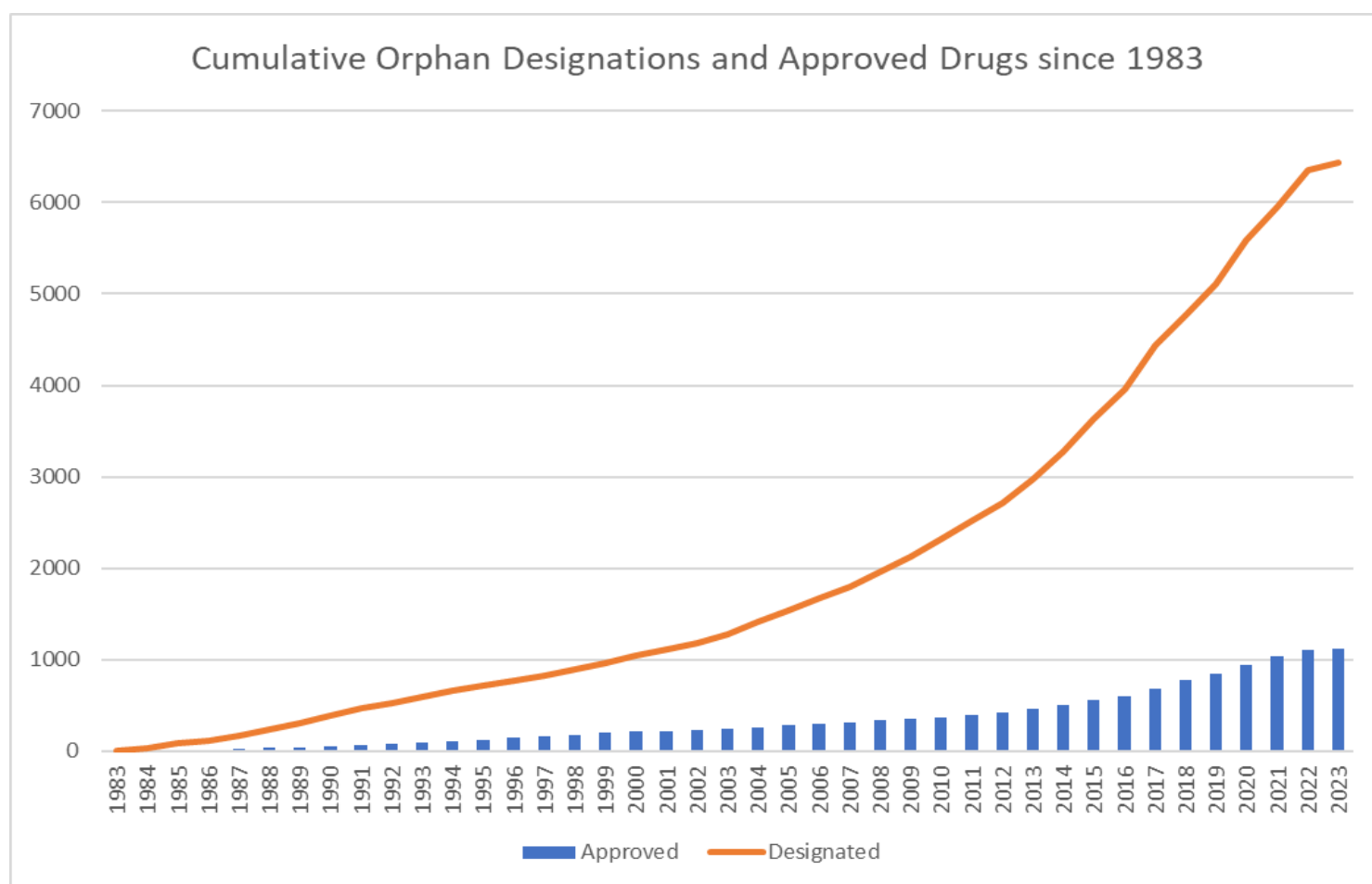
As detailed further, RAAP is extremely concerned about the impact that CMS' final definition of qualified single source drug (QSSD) will have on patients.² With history as a guide, RAAP believes that CMS' final definition of QSSD will have a significant chilling effect on investment in clinical development of orphan drugs.

I. Background: Rare Diseases and Orphan Products

¹ CMS, Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (Mar. 15, 2023), available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>

² *Id.* at page 7.

Over 7,000 rare diseases affect more than 30 million Americans.³ The Orphan Drug Act (ODA), enacted in 1983, provides financial incentives to encourage the development of drugs to treat, diagnose, or prevent rare diseases or conditions that affect fewer than 200,000 people in the US. The ODA has resulted in manufacturers developing orphan drugs that have provided benefit to previously overlooked populations, including new drugs offering breakthrough therapies and existing drugs providing medical benefits for new populations. Since 1983, 6,371 drugs and biologics have received the Orphan Drug designation, and the FDA has approved 1,110 drugs and biologics for orphan indications, as shown in the figure below⁴:



Whereas, from 1973-1983, manufacturers marketed only 34 orphan products, 10 of which were developed by the pharmaceutical industry and 24 were developed from research and funding by the federal government.⁵ This is a stark and distinguishing difference from today that further reinforces the tremendous positive impact of the ODA. Further, from 1983 to 2014, 843 new molecular entities

³ <https://www.fda.gov/patients/rare-diseases-fda>

⁴ FDA. Search Orphan Drug Designations and Approvals. Accessed March 28, 2023.

<https://www.accessdata.fda.gov/scripts/opdlisting/ood/>

⁵ <https://www2.law.umaryland.edu/marshall/crsreports/crsdocuments/RS20971.pdf>

were approved by the FDA, 25% of those were orphan drugs. A study in *Health Affairs* found that the average number of orphan New Molecular Entities (NMEs) approved per year was 7, but from 2010-2014, the average increased to 12.5 further showing the power of the ODA.⁶

Specifically, the ODA has transformed treatments for rare cancers. Between 1983 and 2015, 177 drugs were approved to treat rare cancers. The 177 approvals originated from 1,391 orphan drug designations.⁷ By almost any measure the ODA has successfully achieved its policy objectives—to stimulate the development of orphan therapies.

Rare diseases include more familiar conditions, such as cystic fibrosis, Lou Gehrig's disease, and Tourette's syndrome, as well as less familiar conditions, such as aromatic L-amino acid decarboxylase (AADC) deficiency, Duncan's Syndrome, Madelung's disease, and acromegaly/gigantism. These conditions are complex and often not well understood, which causes great challenges to the diagnosis and treatment as well as research efforts. Rare disease treatments range from curing the disease, modifying how the disease functions, or treating the symptoms. Truly curative treatments are rare. Disease-modifying therapies target the underlying pathology of a disease to prevent it from worsening. Symptomatic treatments seek to temper symptoms or to maintain physical, emotional, and mental functioning. Only 5% of rare diseases have a treatment approved by the Food and Drug Administration (FDA) and for one-third of individuals with a rare disease, it can take between one and five years to receive a proper diagnosis.

The successes mentioned above resulted from significant clinical investment within the backdrop of the financial incentives of the ODA and a healthcare system that could provide equal access to these life altering therapies. Manufacturers invested knowing that there was a potential of seven years of market exclusivity to recoup the billions of dollars of investment.⁸ Companies relied on the ODA to partner with patients to develop the next generation of orphan therapies and now, however, due to CMS' nearsighted definition of QSSD the future of orphan drug discovery is bleak.

II. CMS' Final Definition of Qualified Single Source Drugs Could Irreparably Stunt the Development of Therapies that Treat Rare Disease

In Section 30.1.1 of the Initial Guidance, entitled, "Orphan Drug Exclusion from Qualifying Single Source Drugs" CMS states that it "is considering whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development."⁹ RAAP appreciates this statement and hopes that the Agency reevaluates its final decisions to identify

⁶ <https://www.healthaffairs.org/doi/10.1377/hlthaff.2015.0921>

⁷ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4828121/>

⁸ <https://www.fda.gov/patients/rare-diseases-fda>

⁹ *Id.* at page 11.

“qualifying single source drugs” at the active moiety/active ingredient level and to set the seven or eleven-year clock for purposes of the qualifying single source drug definition on the date of initial FDA approval. RAAP interprets this definition for orphan drugs as not on the date on which a drug loses its status as an excluded orphan drug. RAAP urges CMS to clarify its intent as if true together, these decisions will stunt manufacturer development of orphan drugs because it will force manufactures to choose between developing an orphan indication or a non-orphan indication.

A. CMS’ Overreach Of Defining QSSD based on Active Moiety/Active Ingredient will Disincentivize Orphan Drug Development

In its Initial Guidance, CMS states that “[i]n accordance with the statutory language (section 1192(e)(1) of the Inflation Reduction Act (IRA)) cited above for purposes of the Negotiation Program, CMS will identify a potential qualifying single source drug using: For drug products, all dosage forms and strengths of the drug **with the same active moiety** (emphasis added) and the same holder of a New Drug Application (NDA) inclusive of products that are marketed pursuant to different NDAs. For biological products, all dosage forms and strengths of the biological product **with the same active ingredient** (emphasis added) and the same holder of a Biologics License Application (BLA) inclusive of products that are marketed pursuant to different BLAs.”¹⁰ In other words, the potential qualifying single source drug will also include all dosage forms and strengths of the biological product with the same active ingredient and marketed pursuant to the same BLA(s).¹¹ RAAP believes that Agency’s final policy of combining drugs by active moiety and biologicals by active ingredient is inconsistent with the plain reading of the statute that in turn will harm orphan drug development.

Specifically, the plain text of section 1192(e)(1) references FDA action in the singular, not the plural by using word approval or licensure, not approvals or licensures. The law states that “qualifying single source drug” is defined for products approved under an NDA by reference to whether seven years has elapsed since “such approval.” Similarly, the term is defined for products licensed under a BLA by reference to whether eleven years has elapsed since “such licensure.” These clauses are written in the singular, it therefore requires products to be treated as the same qualifying single source drugs only where they share the same NDA or BLA. The use of “such license” and “such approval” is intentional and unambiguous. Congress used this language to denote that a qualifying single source drug is distinguished by a distinct approval or licensure—i.e., a distinct NDA or BLA. CMS must give effect to the plain language of the statute by distinguishing among qualifying single source drugs based on their FDA application and reverse this final decision.

Biopharmaceutical innovation is incremental, relying on sustained and continuous improvements to molecules, pathways, and modes of administration to achieve

¹⁰ <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf> at page 8.

¹¹ *Id.*

maximum clinical benefit for patients. For patients living with a rare disease or disorder this development process is particularly necessary because of the rarity of their condition. Science cannot take significant leaps and develop new active moieties with each generation of treatment. By combining drugs at the active moiety or active ingredient level, CMS is likely cutting off hundreds of investments into new orphan disease indications.

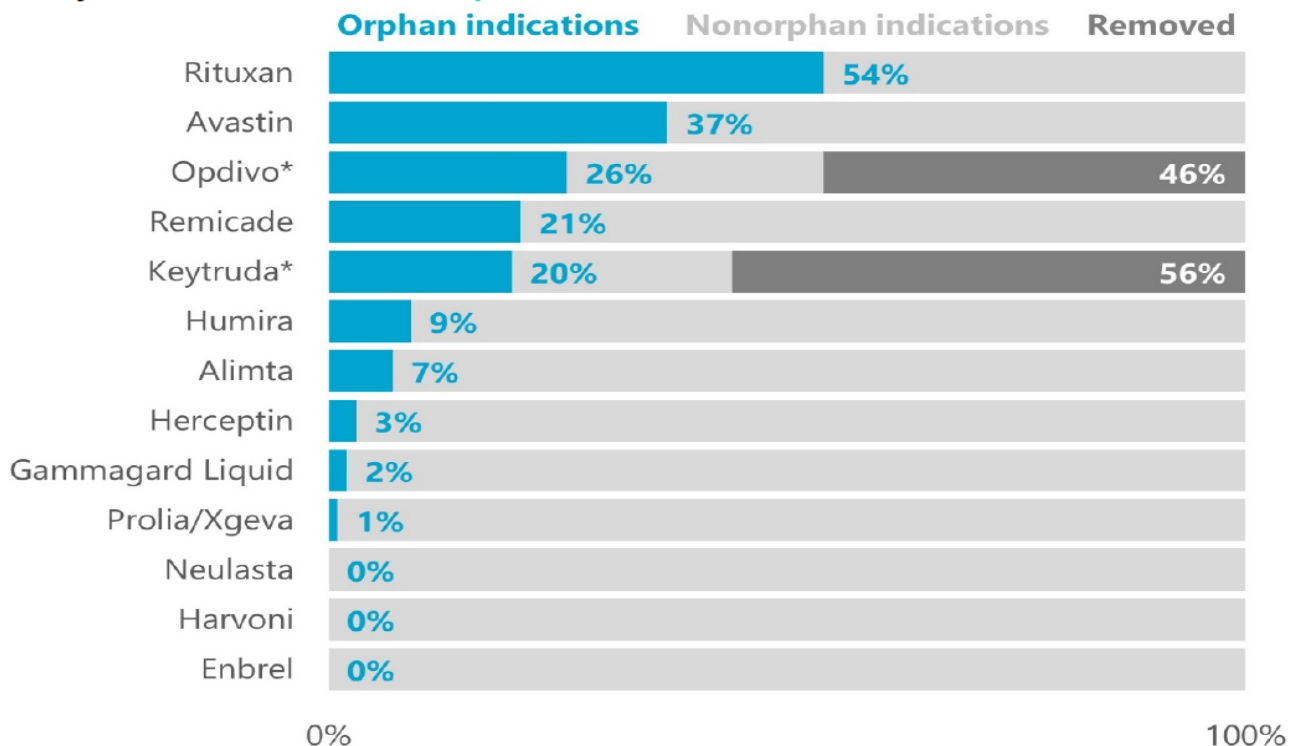
B. CMS' Decision of Starting the Negotiation Clock at FDA Approval will Prevent Clinical Development for Rare Therapies

CMS states that to determine the date of approval or licensure for a potential qualifying single source drug with more than one FDA application number, CMS intends to use the earliest date of approval or licensure of the initial FDA application number assigned to the NDA/BLA holder for the active moiety / active ingredient. Consistent with CMS' request on actions it could take to best support orphan drug development, RAAP strongly urges CMS to reverse this decision and or clarify that for orphan drugs, where a drug loses eligibility for the orphan drug exclusion, the clock starts on the date the drug loses such eligibility, not the date of FDA approval for purposes of the qualifying single source drug definition.

Manufacturers typically seek indications and orphan designations sequentially as new clinical evidence is developed, and thus starting the clock at FDA approval regardless of clinical sequencing will hurt orphan drug discovery. For example, the U.S. Department of Health and Human Services Office of Inspector General, published a report in 2021 that demonstrates the potential impact that this policy could have on orphan drug discovery. Specifically, based on the graph¹² below the orphan indications for the top drugs on the list would likely not have been developed. It is reasonable to believe that the manufacturer of these blockbuster drugs may have chosen only the larger indications.

¹² Id.

Exhibit 6: Drugs with both orphan and nonorphan approvals were much less likely to be used for their orphan indications.



Source: OIG analysis of 2018 Medicare Part B claims and Part D PDE records.

*Note: Opdivo and Keytruda both have FDA approval for orphan indications to treat small cell lung cancer (SCLC), as well as nonorphan indications to treat non-small cell lung cancers (NSCLC). Because ICD-10 diagnosis codes do not distinguish between SCLC and NSCLC, we removed units related to any form of lung cancer from our analysis.

Additionally, RAPP's did a quick review of the FDA database and identified the following ten examples of products that obtained orphan drug designations (ODDs) and received subsequent non-ODD FDA-approvals. Based on CMS' current approach, RAAP believes that none of these orphan indications would have been pursued.

1. Venetoclax originally received approval based on ODD in 2016 for CLL or SLL, and in 2018, received accelerated approval in ND AML under BTD without an ODD.

2. Pembrolizumab originally received approval based on ODD in 2014 for melanoma, and in 2015, received accelerated approval in NSCLC without an ODD

3. Cabozantinib received approval based on ODD in 2017 for HCC, and in 2021, received approval in 1L RCC in combination with nivolumab under FTD and ROTR without an ODD.

4. Atezolizumab received approval based on ODD in 2016 for UC, and in 2018, received approval in 1L NSCLC in combination with bevacizumab and chemo without an ODD.

5. Zanubrutinib received approval based on ODD in 2019 in MCL, and in 2023, received approval in CLL and SLL without an ODD.

6. Olaparib was first approved in 2014 for a subset of ovarian cancer patients. Then it received approval based on ODD in 2019 in pancreatic cancer, and

in 2020, received approval in ovarian cancer in combination with bevacizumab without an ODD.

7. Durvalumab received approval based on ODD in BTC, and in 2022, received approval in NSCLC in combination with tremelimumab without an ODD

8. Pemigatinib received approval based on ODD in 2020 in cholangiocarcinoma, and in 2022, received approval in MLNs without an ODD.

9. Tocilizumab received approval based on ODD in 2021 in systemic sclerosis, and in 2022, received approval for COVID-19 under EUA without an ODD.

10. Ivosidenib received approval based on ODD in 2021 in cholangiocarcinoma, and in 2022, received approval in ND AML in combination with azacitidine under priority review and ROTR without an ODD.

RAAP believes that it is imperative that CMS continue the work of the Congress and the ODA and continue to help stimulate the development of orphan drugs. Through the ODA, Congress devised a regulatory infrastructure that carefully balances incentives in favor of the development of orphan drugs. This history is repeated by Congress in the IRA as evidenced by the orphan drug exclusion. Congress again recognized the special nature of orphan drug discovery. RAAP is disappointed that CMS does not recognize this continued Congressional theme of protecting orphan drug discovery in its final definitions.

As such, RAAP urges CMS to promote orphan drug development by clarifying that the seven- or eleven-year clock for purposes of the qualifying single source drug definition starts on the date on which a drug loses its status as an excluded orphan drug.

III. Other Issues Related to Implementing the Orphan Drug Exclusion

In the spirit of implementing policies that continue to stimulate orphan drug development, RAAP urges the Agency to implement, at a minimum, the following recommendations that will better support ongoing development of and access to drugs targeting patients living with rare diseases.

First, CMS should establish a process that enables manufacturers to submit evidence that an indication falls within an orphan drug designation to account for situations where CMS is unable to determine eligibility for the orphan drug exclusion based on a review of FDA's orphan drug databases. Second, CMS should confirm that it will determine eligibility for the orphan drug exclusion based on orphan drug designation at the time of selection. Under FDA regulations, a manufacturer may voluntarily withdraw a requested or granted orphan drug designation at any time. Where a manufacturer does so, the withdrawal is publicized, and any benefits associated with the designation cease. Accordingly, when determining eligibility for the orphan drug exclusion, CMS should confirm that it will look only to orphan designation at the time of selection and will not look to any prior designation that has been withdrawn. Doing so would help avoid improperly narrowing the universe of protected orphan drugs. Finally, CMS proposes that if a selected drug "has patents and exclusivities that will last a number of years," CMS may adjust the "preliminary price" downward. RAAP is very

concerned by this implication for orphan drug development. Specifically, this could mean that drugs that have orphan exclusivity could have a lower MFP than would otherwise apply further disincentivizing the pursuit of orphan indications.

IV. Conclusion

Based on the policies stated in the Initial Guidance, RAAP anticipates that some if not many of the current drug discovery programs for orphan diseases will unfortunately be discontinued. Therefore, we urge CMS to implement the above changes in order to mitigate the risk that the Initial Guidance will deter the development of these orphan drugs and many more in the future.

Thank you for the opportunity to submit these recommendations on which actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development. RAAP is significantly concerned that without changing the definition of QSSD and starting the clock from when a nonorphan indication is approved that orphan drug discovery will significantly diminish. RAAP believes that CMS owes it to future patients to preserve the intentions and benefits of the ODA and reverse these final decisions regarding the definition of QSSD.

We look forward to working with CMS to further develop policies that maximize access to therapies treating rare diseases. Please feel free to contact me at 202-631-5752 or by email at mike@rareaccessactionproject.org .

Sincerely,

A handwritten signature in black ink, appearing to read "Michael Eging", with a large, stylized circular flourish at the end.

Michael Eging



Rare Disease Company Coalition

BY ELECTRONIC DELIVERY

April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services (CMS)
200 Independence Avenue, S.W.
Washington, DC 20001

RE: Inflation Reduction Act (IRA) Initial Program Guidance; Comment Request (Docket No. CMS-1800-NC2)

Dear Administrator Brooks-LaSure:

The Rare Disease Company Coalition ([RDCC](#)) appreciates the opportunity to provide comments to the Centers for Medicare & Medicaid Services (CMS) initial guidance for the Medicare Drug Price Negotiation Program for the implementation of the *Inflation Reduction Act* (IRA). The RDCC appreciates that the Centers for Medicare & Medicaid Services is considering whether there “are additional actions the agency can take” in implementing the IRA Negotiation Program to “best support orphan drug development.” We recommend that CMS take all possible steps to better support the development of important new orphan drugs, including clarifying key aspects of the Orphan Drug Exclusion.

The RDCC is a coalition of 20 life science companies committed to changing the paradigm in rare disease treatment by discovering, developing, and delivering life-changing therapies for rare disease patients around the globe. To date, RDCC members have brought 45 treatments to market – the majority of which are the first FDA-approved treatments available for a given disease – and have over 200 rare disease treatments in development.

State of Rare Disease Therapy Development and Challenges

In the United States, a rare disease is a condition affecting fewer than 200,000 people. There is an estimated baseline of more than 7,000 individual rare diseases that cumulatively affect about 30 million people in the US, however; this number may be closer to 10,000 individual conditions.¹ These diseases are devastating and often life-threatening: 80 percent of rare diseases are genetic in origin, 50 percent

¹ Haendel, Melissa et al. How many rare diseases are there? NIH National Library of Medicine. <https://pubmed.ncbi.nlm.nih.gov/32020066/>. February 2020.

impact children,² with many rare diseases resulting in premature deaths of infants and young children.³ Despite significant advancements in the detection and sequencing of rare diseases, as well as advances in the development of rare disease therapies, there remains a high unmet need for rare disease patients with at least 95% of rare diseases left without an FDA-approved treatment.

The latter point is a stark reminder of the challenges facing sponsors of rare disease therapies. The investment required to bring an innovative therapy to patients is substantial and requires the application of significant resources toward new technologies, platforms, and treatments. It is estimated that each newly approved drug takes over 10–15 years to develop, and over \$1–2 billion in average costs.⁴ These estimates are in part due to the high degree of resources attributed to the over 90% of drug candidates that fail prior to entering clinical studies, during phase I, II, or III trials, or final approval.⁵ Many of these interventions never make it to market but nonetheless support learning and development to be applied to successful future pursuits. RDCC's 20 members alone invest, on average, over \$15 billion in research and development (R&D) annually.

Legacy of the Orphan Drug Act

Signed into law in 1983 to recognize the need for investment and discovery in the rare disease space, the *Orphan Drug Act* (ODA)⁶ recognized the paucity of rare disease drug development and the need for a series of economic incentives to encourage the development of orphan drugs (a reference to the unwillingness of drug companies to adopt these drugs and take them through the long FDA process). These incentives included tax credits for qualifying clinical trial expenses, exemption from standard user fees attached to new drug and biologic product applications, and eligibility for seven years of market exclusivity post-approval. These incentives have succeeded in increasing the number of approved drugs and biologics to prevent, diagnose, or treat rare diseases and conditions where the total affected patient population is low and where the chance of market failures is due to a reduced ability to recoup research and development costs.

The ODA has demonstrated overwhelming evidence of its success. Before 1983, only 38 drugs were approved to treat rare diseases. Since the passage of the Orphan Drug Act, more than 7,000 rare diseases have been identified, and over 1,100 orphan indications for treatments have obtained FDA approval.⁷ Accordingly, Congress and agencies should continue to explore ways to protect the ODA incentives and further encourage development through guidance and incentives based on changes in the evolving market to ensure that innovation continues for rare disease patients.

² Global Genes. RARE Disease Facts. Global Genes. <https://globalgenes.org/learn/rare-disease-facts/>. Accessed April 14, 2023.

³ National Organization for Rare Disorders. Rare Disease Facts. NORD. <https://rarediseases.org/wp-content/uploads/2019/02/nord-rareinsights-rd-facts-2019.pdf>. 2019.

⁴ Wouters, Oliver et al. Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. *Jama Network*. <https://jamanetwork.com/journals/jama/fullarticle/2762311>. March 3, 2020.

⁵ Sun, Duxin et al. Why 90% of clinical drug development fails and how to improve it? *ScienceDirect*. <https://doi.org/10.1016/j.apsb.2022.02.002>. July 2022.

⁶ [Public Law 97-414](#).

⁷ National Organization for Rare Disorders. The Orphan Drug Act Turns 40: NORD Celebrates Its Impact on Rare Diseases. NORD. <https://rarediseases.org/the-orphan-drug-act-turns-40-nord-celebrates-its-impact-on-rare-diseases/>. January 4, 2023.

Inflation Reduction Act Impact on Rare Disease Drug Development

The recently-signed *Inflation Reduction Act* (IRA) exempts some orphan drugs from Medicare price negotiation. Specifically, the IRA includes a provision that must exclude from price negotiation "a drug that is designated as a drug for only one rare disease or condition under section 526 of the *Federal Food, Drug and Cosmetic Act* and "for which the only approved indication (or indications) is for such disease or condition."⁸ The congressional intent of the Orphan Drug Exclusion was to continue to incentivize drug development for rare diseases by *not* having products that treat rare diseases subject to price controls. On its face, the Orphan Drug Exclusion is an important step in ensuring consistency in the regulation of orphan products in the future, given the lengthy timeline required for advanced therapeutic development. However, while the IRA clarifies that an orphan drug with one designation is excluded from price negotiation, it would disincentivize drug companies from doing further research to develop a rare disease drug for additional rare diseases by making that product eligible for negotiation once they have obtained a second designation. Notably, orphan drugs are often later approved for additional therapeutic areas, and if that happens, the IRA will no longer exempt them from price negotiations.

This approach also fails to account for important advances in drug development, stifling innovation through isolating single indications. For instance, Section 504 of the *Food and Drug Administration Reauthorization Act of 2017* (FDARA) required pediatric assessments to be made on adult drugs based on the claimed indication of the drug and the relevant molecular target for pediatric cancer drugs.⁹ This legislative change has resulted in FDA's creation of lists of molecular target candidates in multiple categories. Such a change, long discussed by stakeholders as a means of generating new drug studies in the pediatric population, indicates a significant change in how drugs are developed and expands the possibility of repurposing drugs with existing rare disease indications to others. According to an IQVIA/NORD report from December 2020 that examines trends in rare disease innovation, "there are 447 drugs with orphan-only indications, with 104 drugs approved for two or more orphan indications. Compared with the development of novel orphan drugs, repurposing drugs for new indications is a time-saving and cost-efficient method resulting in higher success rates, which can, therefore, drastically improve drug development for rare diseases.

The existing exemption is confined to a narrow set of orphan medicines. It raises the question of the extent to which innovation in rare disease development for indications for other rare diseases will be affected by Medicare drug price negotiations. This framework would achieve the opposite of the intended purpose of the aforementioned ODA, which is to encourage the development of drugs for rare diseases by providing incentives in the form of regulatory exclusivity.

As a result of this policy, companies will be forced to make hard choices regarding R&D investment. Remaining uncertainty about if, when, and how rare disease drugs will become negotiation eligible creates business risks that disincentivize the development of drugs for the limited populations impacted by rare diseases. Since the passage of the IRA, companies have already announced plans to suspend their additional orphan indication programs in light of the narrowness of the orphan drug exemption, highlighting the real-world impact that this legislation is already having on orphan drug R&D and investment.¹⁰ Even before a drug reaches the negotiation list, due to the complexity and long timeline

⁸ Section 1192(e)(3)(A); [Public Law 117-169](#).

⁹ [Public Law 115 - 52](#).

¹⁰ Kelly, Cathy. IRA Effect: Alnylam Acting 'Rationally' In Halting Second Orphan Indication For Amvuttra – Analysts. Pink Sheet. <https://tinyurl.com/bdh8cbrf>. November 7, 2022.

from initial drug discovery and early R&D to full FDA approval, these suspension decisions are being made now as investors and companies look to minimize their risk. These decisions will impact the drug development pipeline for decades to come.

Given the current construct of the law, timing issues are crucial for sponsors to understand the horizon for drug development and how the IRA provisions may impact their market viability in the future. As CMS considers whether there are additional actions the agency can take in its implementation of the Negotiation Program to best support orphan drug development, CMS should clarify that obtaining additional designations for a small molecule or biologic will not make a drug negotiation eligible until the drug has been approved by the FDA for seven or 11 years to treat the second disease or condition (i.e., the date the exemption ends rather than the date of FDA approval for the original orphan indication) and in doing so, would provide meaningful incentives for continued rare disease drug development. Further, CMS must clarify that the timeline for negotiation eligibility would begin for a product that no longer qualifies for the Orphan Drug Exclusion upon approval for another condition.


Recommendations

In summary, as CMS considers whether there are additional actions it can take in implementing the Negotiation Program to best support orphan drug development, RDCC urges CMS to:

- Ensure rare disease drug development is not stifled; we request that CMS clarify that obtaining additional orphan designations for a small molecule or biologic will not make a drug negotiation eligible until the drug has been approved by FDA for 7 or 11 years to treat the second disease or condition.
- Clarify that where an orphan drug loses eligibility for the orphan drug exclusion, the 7- or 11-year “qualified single source drug” clock runs from the date on which the drug lost eligibility for the exclusion.

We appreciate the Agency’s attention to these important issues and urge immediate action to strengthen protections and certainty for those developing rare disease therapies. Should you have any questions, please feel free to contact me at amanda@rarecoalition.com.

Sincerely,

A handwritten signature in cursive script that reads "Amanda Malakoff". The signature is written in dark ink on a light-colored background.

Amanda Malakoff
Executive Director
Rare Disease Company Coalition



April 14, 2023

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Allies for Health + Wellbeing

Dr. Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health & Human Services
Hubert H. Humphrey Building
Independence Avenue, SW
Washington, DC 20201

VIA EMAIL to: IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Dr. Seshamani:

RWC-340B appreciates the opportunity to submit comments to the Centers for Medicare & Medicaid Services ("CMS") on the guidance Memorandum entitled "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments" ("Memorandum"). Our comments concern Section 90.2 of the Memorandum: "Monitoring of Access to the MFP."

As background, RWC-340B is a national association of HIV/AIDS health care clinics and service providers receiving support under the Ryan White Comprehensive AIDS Resources Emergency ("CARE") Act. Ryan White clinics are dedicated to caring for low-income and vulnerable patients living with HIV/AIDS and are serving on the frontlines of both the AIDS epidemic and the COVID pandemic, supporting high risk clients and communities. RWC-340B members provide primary care, case management, and other support services for persons living with HIV/AIDS. For many of these services, Ryan White clinics receive little to no compensation and, for that reason, are highly dependent on the 340B drug pricing program ("340B Program") to underwrite the cost of providing comprehensive care to their patients.

RWC-340B supports CMS's objective to implement the requirement of the Inflation Reduction Act of 2022 ("IRA"), including a manufacturer's obligation to provide 340B safety net providers the difference between the maximum fair price ("MFP") and the 340B ceiling price when the MFP is lower than the 340B ceiling price. RWC-340B has two comments.

First, CMS states that it will make available on a publicly available website: the selected drugs, initial price applicability years, the MFP files, and the explanations of factors having the greatest influence on

determining the MFPs.¹ RWC-340B supports CMS's decision to make publicly available all MFP prices and relevant supporting information. Providing the MFP price publicly ensures that the important process of comparing the MFP and 340B ceiling price is fair and transparent. We request that CMS ensure that the MFP pricing information is presented in a format that is consistent with and easily comparable to the ceiling price information on the Office of Pharmacy Affairs Information System (OPAIS).

Second, with respect to access to the MFP for 340B covered entities, the IRA states that a manufacturer "shall be required to provide access to the maximum fair price to such covered entity with respect to maximum fair price eligible individuals who are eligible to be furnished, administered, or dispensed such selected drug at such entity at such ceiling price in a nonduplicated amount to the ceiling price if such maximum fair price is below the ceiling price for such selected drug." 42 U.S.C. § 1320f-2(d)(2). In two instances in the memorandum, however, CMS states that a manufacturer must give a 340B covered entity the difference between the 340B price and the MFP "[i]f the 340B ceiling price is subsequently determined to be lower than the MFP."² These statements appear to be an error and RWC-340B requests that CMS correct this mistake.

* * *

RWC-340B appreciates the opportunity to provide input on this important issue. Thank you for your consideration of our comments. If you have any questions, please feel free to reach out to me at ceo@cempa.org.

Sincerely,



Shannon Stephenson
President
RWC-340B

¹ CMS, Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments at 60 (Mar. 15, 2023), <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

² *Id.* at 33, 66 (Sections 40.4 and 90.2).



April 14, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201_
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Sana Biotechnology, Inc. (Sana) appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

About Sana Biotechnology, Inc.

Sana is focused on creating and delivering engineered cells as medicines for patients. We share a vision of repairing and controlling genes, replacing missing or damaged cells, and making our therapies broadly available to patients. We are a passionate group of people working together to create an enduring company that changes how the world treats disease. Sana is a U.S. company with operations in Seattle, WA, Cambridge, MA, South San Francisco, CA and Rochester, NY.

Sana has developed a hypoimmune platform designed to create cells *ex vivo* that can “hide” from the patient’s immune system to enable the effective transplant of allogeneic cells. We are applying hypoimmune technology to donor-derived allogeneic T cells, with the goal of making potent and persistent CAR T cells at scale. Autologous CAR T cells have shown tremendous potential, but are difficult to make, challenging to deliver, and variable in product quality. Allogeneic CAR T cells have generally disappointed to date, as the challenge of immune rejection of foreign cells has limited the durability of patient responses. Our goal is simple – clinical benefit at least as good as that achieved with autologous CAR T cells on the most meaningful outcome for patients, durable complete responses (no evidence of cancer), with a scale, product consistency, and deliverability comparable to a regular drug. Our most advanced program using hypoimmune technology is SC291, our hypoimmune CD19-targeted allogeneic CAR T therapy, targeting cancers such as acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), and non-Hodgkin’s lymphoma (NHL). Our preclinical data highlight that these hypoimmune CAR T cells can evade immune detection, persist, and clear tumor cells both acutely and over time. If these results translate to our clinical studies, SC291 has transformative potential for patients, and we look forward to presenting initial clinical data later this year. SC291 is the first drug to enter the clinic from Sana’s HIP CAR T platform; this platform has the potential to create a regenerative pipeline for allogeneic



CAR T therapies. After SC291, our next programs using hypoimmune technology include our allogeneic CD22-targeted CAR T program targeting ALL, CLL, NHL cancers and our allogeneic BCMA-targeted CAR T program targeting multiple myeloma.

Currently, allogeneic T cells derived from human whole blood are used to manufacture our allogeneic CAR T cell therapies. If ultimately approved as biological products under section 351(a) of the Public Health Service Act, Sana's allogeneic CAR T cell therapies will be biological products derived from human whole blood.

Summary of Comments

We are requesting that CMS revise to the Drug Price Negotiation Program Guidance to make clear that any biological product licensed under section 351(a) of the Public Health Service Act and derived from human whole blood or plasma will be excluded when identifying drugs to be included in the Medicare Drug Price Negotiation Program, consistent with the statute. The statutory exclusion for plasma-derived products in the Inflation Reduction Act (IRA) is both clear and broad in the exclusion. We believe that the Drug Price Negotiation Program Guidance, if not revised, creates an ambiguity in which drugs are subject to this exclusion, which could be construed as limiting the statutory exclusion. This discrepancy between the statute and guidance creates uncertainty for innovator companies like Sana, magnified by the pipeline nature of our development, which can ultimately decrease the development of innovative medicines for patients. In addition, the deviation from the clear language of the statute is arbitrary and capricious and will inevitably lead to litigation. This will divert resources of both innovators and the agency from the development and delivery of medicines to patients.

Section 30.1.3 Comments

Specifically, the IRA defines Plasma-Derived Products as "A biological product that is derived from human whole blood or plasma" and the IRA provides that a biological product is (in relevant part) one "licensed under the section 351(a) of the Public Health Service Act". In other words, to the extent a biological product is licensed under a BLA and is derived from human whole blood or plasma, it falls into the plain language of the Plasma-Derived product exclusion in the statute.

In contrast, the Drug Price Negotiation Program Guidance adds additional criteria to this exclusion that narrows which products would qualify for the exclusion. The guidance states that CMS "will refer to product information available on the FDA Approved Blood Products website to identify approved blood products regulated as biological products and the FDA Online Label Repository to verify if the product is derived from human whole blood or plasma." This guidance creates an ambiguity suggesting that the sole place to look for biological products meeting the Plasma-Derived product exclusion is the FDA Approved Blood Products website. This impermissibly narrows the statutory exclusion, which simply requires the biological product to be approved via a BLA and be derived from human whole blood or plasma.

Therefore, we request that CMS revises its guidance to reflect the clarity and breadth of the Plasma-Derived Products statutory exclusion of the IRA. Failure to do so would be inconsistent with the statute and would be arbitrary and capricious. Specifically, we ask that revisions be made to the Drug Price Negotiation Program Guidance as follows:



- (i) make clear that any biological product licensed under section 351(a) of the Public Health Service Act and derived from human whole blood or plasma will be excluded by CMS when identifying drugs to be included in the Medicare Drug Price Negotiation Program;
- (ii) make clear that the FDA Approved Blood Products website is only one way, and not the only way, to identify approved blood products regulated as biological products;
- (iii) make clear that the approved biological product's labeling is the means to verify if the product is derived from human whole blood or plasma, including through consultation with FDA as needed.

* * * * *

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to patients from fewer innovative medicines is minimized. Please contact Jennifer Tousignant by telephone at (206)701-7914 or by e-mail at jennifer.tousignant@sana.com, if you have any questions regarding our comments.

Sincerely,

DocuSigned by:

EA83C0489296466...
Jennifer Tousignant
Senior Vice President, Legal
Sana Biotechnology Inc.
300 Technology Square, Cambridge, MA 02139

April 14, 2023

VIA ELECTRONIC DELIVERY to: IRAREbateandNegotiation@cms.hhs.gov

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244-1850

RE: Medicare Drug Price Negotiation Program Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026: Response to Solicitation of Comments

Dear Administrator Brooks-LaSure:

Seagen Inc. appreciates the opportunity to comment on the Medicare Drug Price Negotiation Program: Initial Memorandum (initial guidance) issued by the Center for Medicare & Medicaid Services (CMS or Agency) on March 15, 2023.¹

Seagen is a global biotechnology company that develops and commercializes transformative cancer therapies. Seagen's singular mission is to make a difference for people impacted by cancer. As an industry leader in antibody drug conjugate (ADC) technology, we pioneered the science of harnessing antibodies designed to deliver cell-killing agents to cancer cells. Three of four of our approved medicines are built on this technology. Seagen has a deep and diverse pipeline of next-generation ADC technologies, small molecule, and other targeted therapies aimed at addressing unmet needs of people living with cancer.

¹ Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year (IPAY) 2026, and Solicitation of Comments.

Targeted cancer therapies, like the ADCs manufactured by Seagen, are designed for very specific patient populations, expensive to develop, and difficult to manufacture. Uncertainty in future returns creates significant risk to future patient access by reducing our ability to reinvest in our pipeline. In 2022, Seagen invested \$1.3 billion into research and development and \$1.2 billion in 2021. There are other smaller manufacturers making deep investments in transformative cancer therapies. However, due to government price setting, companies like Seagen will be forced to walk away from gaining initial approvals in smaller patient populations, often in later lines of therapy where disease has progressed and prognosis is grim. Studies have demonstrated that government price setting is associated with dramatic declines in early research and patient access, which, of course, is the fundamental precursor to a robust and growing pipeline of new therapies targeting areas of unmet medical need, including cancer therapies.²

The initial guidance only relates to the Program for IPAY 2026, and it is critical CMS provides additional guidance following the complete rulemaking with comment period for IPAY 2028, which will apply to Part B products in addition to Part D products. Due to the limited scope of this initial guidance, CMS is missing critical stakeholder feedback on complex issues impacting Part B drugs, like utilization of J-codes as a more appropriate way to identify potentially qualifying single source physician-administered products and other nuances not addressed within the current guidance. With additional time ahead of implementation for Part B, Seagen urges CMS to follow the standard rulemaking process.

As a threshold matter, Seagen is concerned that CMS did not solicit comment on Section 30 of the initial guidance, which includes important guidance regarding the definitions of qualifying single source drugs and negotiation-eligible drugs, which form the basis of the Program. We believe CMS's failure to request comment on these provisions removes an important opportunity for public input on the foundations of CMS' implementation of the program. In addition, Seagen requests the Agency not only solicit comments on the entirety of initial guidance, but also review and consider all comments provided by stakeholders regarding such guidance.

It is important to clarify the process Congress describes as a "negotiation" under the Program is not a true negotiation. The Program lacks clear communication between impacted parties, reasonable opportunity for manufacturer input, and most importantly lacks ability for impacted stakeholders to identify and correct errors which prohibits mutual assent. Instead, Congress describes price setting under the veil of negotiation,

² See T. Abbott & J. Vernon, *The Cost of US Pharmaceutical Price Reductions: A Financial Simulation Model of R&D Decisions*, 28 Managerial & Decision Econ. 293 (2007); see also Vital Transformation, *The Historical Impact of Price Controls on the Biopharma Industry* (2021), <https://vitaltransformation.com/2021/11/the-historical-impact-of-price-controls-on-the-biopharma-industry/>.

and Seagen urges CMS to use its implementation authority to make the Program a more equitable and transparent process for all stakeholders.

I. Qualifying Single Source Drugs and Negotiation-Eligible Drugs

A. Seagen strongly encourages CMS to define a Qualifying Single Source Drug as encompassing a single New Drug Application (NDA) or single Biologics License Application (BLA) in alignment with statute.

Section 1192(e) of the Social Security Act (SSA) generally defines “qualifying single source drug” to mean:

- A drug product “that is approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act [FDCA] and is marketed pursuant to such approval” where “at least seven years have elapsed since the date of such approval” and “that is not the listed drug for any [generic] drug that is approved and marketed”;³ and
- A biological product “that is approved under section 351(a) of the Public Health Services Act [PHSA] and is marketed under section 351(a) of such Act where at least eleven years has elapsed since the date of such licensure” and “that is not the reference product for any [biosimilar] biological product that is licensed and marketed.”⁴ The statute provides for limited exclusions from this definition for certain orphan drugs, plasma-derived products, low Medicare-spend drugs, as well as an exclusion for small biotech drugs under the definition of negotiation-eligible drugs.

Under the initial guidance for biologics, CMS proposes to identify a qualifying single source drug as all dosage forms and strengths with the same active ingredient and the same BLA holder, “inclusive of products that are marketed pursuant to different BLAs. CMS intends to apply a similar approach to drug products. We urge CMS to identify a qualifying single source drug by reference to a single NDA or BLA. Under statute, “qualifying single source drug” is defined for products approved under an NDA or BLA by reference to whether enough years has elapsed since “such approval”⁵ or “such licensure,”⁶ respectively.

By using these terms which refer to an “approval” and a “licensure” in the singular, the statute clearly defines qualifying single source products by a single distinct NDA or BLA. There is no alternative definition

³ SSA § 1192(e)(1)(A) (the seven years are counted to the selected drug publication date with respect to the applicable initial price applicability year (IPAY)).

⁴ *Id.* § 1192(e)(1)(B) (the eleven years are counted to the selected drug publication date with respect to the applicable IPAY).

⁵ SSA § 1192(e)(1)(A).

⁶ *Id.* § 1192(e)(1)(B).

supported by the language or intended by Congress. Therefore, CMS must adopt the same definition when identifying single source drugs under the Medicare Drug Price Negotiation Program.

Additionally, by following the plain language of the statute identifying a single source drug by reference to the individual NDA or BLA, the associated dosage forms and strengths, across which Medicare expenditures are aggregated and the MFP applied, must also be referenced to the assigned NDA or BLA of said product. In a letter to the Agency, certain members of Congress call this “an apparent effort to subject as many medications as possible to the IRA’s price-setting program” by using “an unusual definition of ‘qualifying single-source drugs’ that aggregates entirely different medications according to their active ingredient or moiety, thereby discouraging research into future drug indications.”⁷ As the Agency’s initial guidance constitutes overreach, CMS must correct its approach to align to the statute by specifying that for purposes of aggregation of Medicare expenditures and application of the MFP, dosage forms and strengths are also identified by reference to the NDA or BLA of the qualifying single source.⁸

II. Orphan Drugs

A. Seagen encourages CMS to exclude products with multiple orphan indications, where all indications for a given product are orphan.

The Inflation Reduction Act categorically excludes a drug from negotiation eligibility if the drug is “designated as [an orphan drug] for only one rare disease or condition . . . and . . . the only approved indication (or indications) is for such disease or condition.”⁹ In an attempt to reach the most patients who could benefit from a therapy, it is not uncommon for a single product to be tested and approved for use in multiple orphan diseases. Due to the inherent complexities in developing drugs for orphan diseases, where a single product provides benefit to more than one orphan disease, under the current statute that drug or biologic receives no protection from Medicare price negotiation. This harms all patients – whether orphan disease or otherwise – who are waiting for breakthroughs while simultaneously disincentivizing manufacturers from pursuing additional trials for products that already serve a separate orphan disease.

⁷ Republican letter to the Agency on April 12, 2023, available at https://www.finance.senate.gov/imo/media/doc/sfc_ira_price-setting_program_implementation_guidance.pdf

⁸ Regardless of the “qualifying single source drug” definition adopted by the Agency, CMS must **consistently** apply such definition. As such, if CMS were to maintain that products that share the same active moiety (drugs) or the same active ingredient (biologics) are the same qualifying single source drug, BIO agrees that the market entry of a generic or biosimilar to **any** such product would disqualify **all** such products from treatment of a qualifying single source drug. See Initial Guidance at 10. Any other approach would be irreconcilable with CMS’s stated “qualifying single source drug” definition. See, e.g., *Nat’l Credit Union Admin. v. First Nat. Bank & Tr. Co.*, 522 U.S. 479, 501–02 (1998) (a basic canon of interpretation is that similar or identical language “be accorded a consistent meaning”).

⁹ SSA § 1192(e)(3)(A) (such drugs are categorically ineligible for selection for negotiation because they are excluded from the definition of “qualifying single source drug”).

B. CMS should clarify that, where an orphan drug loses eligibility for the orphan drug exclusion, the seven- or eleven-year “qualified single source drug” clock runs from *the date on which the drug lost eligibility for the exclusion*.

Doing so would help maximize protection for orphan drugs. Absent such clarification, an orphan drug that loses eligibility for the orphan drug exclusion could be virtually immediately subject to selection for negotiation, simply because it was designated as an orphan drug for a second rare disease, or an indication was approved for a second disease. CMS should act to avoid such a result, as it would further disincentivize developers of orphan drugs from investing in treatments for orphan diseases.

Implementing the above recommendations is necessary to mitigate the risk that the Program will deter the development of orphan drugs to treat those suffering from rare diseases. It is also fully consistent with long-standing Congressional policy favoring protection of orphan drugs. The orphan drug exclusion is merely the latest of a long line of Congressional policies protecting orphan drugs. Such policies date back to the early 1980s, when Congress enacted the Orphan Drug Act of 1983 to create various incentives to encourage and facilitate the development of new orphan drugs.¹⁰ In keeping with Congress’s long-held policy of protecting orphan drugs, CMS should make every effort to ensure that it does not hamper orphan drug innovation as it implements the Program and its orphan drug exclusion.

III. Selection Process for Negotiation

A. CMS must adopt a clear appeal process for stakeholders to request additional consideration or review of CMS selection decisions.

For each IPAY, the statute directs CMS to publish a list of the drugs that have been selected for negotiation (under statutorily specified parameters) by February 1 of the year that is two years before such IPAY (with a modified timeline for IPAY 2026).¹¹

Although the Inflation Reduction Act contains limits on administrative and judicial review of certain determinations, CMS still has significant discretion in establishing procedures to resolve disputes and correct errors that arise during the MFP decision-making process. Seagen strongly urges CMS to exercise its discretion and adopt an early-notice and dispute resolution process at least 12 months prior to intended selection of a drug or biologic for negotiation, consisting of both notice of selection intent and anticipated non-FAMP ceiling, to afford due process and ensure the integrity of the Program for future IPAYs. Eligibility

¹⁰ See Orphan Drug Act, Pub. L. No. 97-414, §§ 1, 2, 96 Stat. 2049, 2049–51 (1983), as amended by Pub. L. 98-551, 98 Stat. 2815, 2817 (1984).

¹¹ SSA §§ 1191(b)(3), 1192(a); see also *id.* § 1191(d)(1) (September 1, 2023, for IPAY 2026).

for selection is based on multiple factors, including whether a sufficient number of years have elapsed since approval or licensure;¹² whether a generic or biosimilar has come to market;¹³ whether the drug is eligible for the orphan drug exclusion;¹⁴ whether the drug is a plasma-derived product;¹⁵ whether the drug is a small biotech drug;¹⁶ whether Medicare expenditures are sufficiently low to disqualify the drug from selection;¹⁷ and whether Medicare expenditures are sufficiently high to qualify the drug for selection.¹⁸

Additionally, CMS intends to require manufacturers to submit newly approved NDC-11s, as well as delisting existing NDC-11s within 30 days of marketing discontinuation for the calculation of total expenditures. This is yet another area where manufacturers must be able to identify and correct errors in this list to avoid under- and misattribution by CMS.

Implementation of the Inflation Reduction Act is complex, and without the inclusion of a robust process for manufacturers to provide input and suggested corrections it will be easy for errors to be made. In fact, mistakes already have been made by the Agency during Inflation Reduction Act implementation. Specifically, the Medicare Part B Inflation Rebate beneficiary coinsurance reduction amounts were calculated and published in error (we believe due to use of the incorrect reference quarter)¹⁹. This mistake underscores the critical need for stakeholders to be able to identify and request correction of future errors, particularly since errors within the negotiation program could easily lead to significantly reduced patient access.

IV. Negotiation Process

A. Seagen recommends specific steps to improve the proposed negotiation process.

The statute requires CMS to “develop and use a consistent methodology and process...for negotiations” of the MFP.²⁰ Congress intended for the negotiation process to be transparent and predictable for all participants, and although no two negotiations will be alike, every negotiation should be subject to a clear and reasonable assessment framework. The framework should be published with public comment solicited

¹² *Id.* § 1192(e)(1).

¹³ *Id.*

¹⁴ *Id.* § 1192(e)(3)(A).

¹⁵ *Id.* § 1192(e)(3)(C).

¹⁶ *Id.* § 1192(d)(2).

¹⁷ *Id.* § 1192(e)(3)(B).

¹⁸ *Id.* § 1192(d)(1).

¹⁹ Reduced Coinsurance for Certain Part B Rebatable Drugs under the Medicare Prescription Drug Inflation Rebate Program, Centers for Medicare and Medicaid Services, <https://www.cms.gov/files/document/reduced-coinsurance-part-b-rebatable-drugs-apr-1-june-30.pdf> (last visited April 5, 2023).

²⁰ SSA § 1194(b)(1). The renegotiation process must be consistent with the negotiation process to the extent practicable. *Id.* § 1194(f)(1), (4).

and incorporated by the Agency, and should be applicable to all negotiations, both initial and all renegotiations.

Additionally, because each negotiation will necessarily be unique, assessments for oncology products should be completed for each indication, considering each patient population, disease state, and line of therapy, in alignment with the label prescribing information. Cancer is different and cannot be equated to diabetes, asthma, autoimmune diseases, or other chronic diseases. Assessment and review of individual oncology products must consider the targeted nature of the therapy, including the disease state, patient population, line of therapy, and any biomarker considerations. Due to these complexities, targeted cancer therapies, like the ones manufactured by Seagen, must receive individual review at the individual NDA, BLA or NDC-11/J-code level. This review should include the input of a therapeutic-assessment advisory committee inclusive of medical professionals with representation across specialties to ensure appropriate consideration of all factors throughout the negotiation process. An informed panel must include physician representation with deep experience treating in the specialty (such as oncologists for oncology selected drugs), health economists, and patient representation from the specialty. Such an approach will ensure differences between disease states, patient populations, and medical need are assessed appropriately and further Congress and CMS's shared goal of protecting patient access.

B. Seagen asks CMS to consider research and development costs appropriately.

Regarding the negotiation factors submitted by manufacturers in accordance with section 1194(e)(1) of the Act, Research and Development Costs should include drug development platform costs associated with the development of the selected drug. Additionally, to protect and encourage innovative drug development, Research and Development Costs should include the cost of development of drugs in which development was discontinued at a ratio of the manufacturers reinvestment rate of revenue to drug development costs in the therapeutic area of the selected drug.

C. Seagen requests the Agency allow flexibility in the submission of manufacturer information and allow additional engagement between negotiating parties.

Since individual circumstances of a selected product will vary and may not be identified in advance for every possible future negotiation, the Agency must afford flexibility to manufacturers by allowing submission and due consideration of all forms of clinical, health economic and outcomes research (HEOR), real world evidence (RWE), patient reported outcomes (PROs), and other additional evidence deemed relevant and meaningful by the manufacturer. Related, as all evolving market dynamics may not be anticipated, a manufacturer should also be permitted to supplement its timely submission where a post-submission development arises or there otherwise is good cause. It is vital that CMS allow such submissions after the

submission deadline. In addition to allowing for such submissions, the Agency must include supplemental information in its assessment of the product.

Furthermore, at any point in the offer and counter-offer process, either the manufacturer or CMS should be allowed to request confidential live or virtual engagements to ensure transparency in the assessment of products assessed for negotiation.²¹ Following an assessment process which includes these critical steps is not only statutorily required but also helps to ensure that CMS complies with its legal obligation to treat similarly situated entities similarly, absent a reasoned basis for distinction.²²

D. To support clarity in the Medicare Drug Price Negotiation Program, CMS should provide *meaningful justification* of its initial offer or any counteroffer. CMS must also provide the manufacturer with enough time for response during the negotiation process.

Open dialogue will be vital to the transparency of the Program. To this end, Seagen asks CMS to specify that its initial offers and its responses to any counteroffers include *meaningful* explanations of how the Agency arrived at the offer or response. *Meaningful explanations* should include the citing of any sources CMS used in its review.

In addition, as part of a negotiation process, both CMS and manufacturers should be afforded the same amount of time for review and submission of initial and/or subsequent offers. Seagen respectfully requests CMS commit to responding to any counteroffer within 30 days. We further ask CMS to commit to affording at least 30 days for manufacturers to comment on the response and for CMS to consider any such comment before the MFP is set. Such protections are essential to ensuring the integrity of a sustainable negotiation process.

E. Seagen requests CMS protect the confidentiality of any proprietary information submitted in the course of negotiation.

The statute imposes a clear confidentiality requirement: “Information submitted to . . . [CMS] . . . by a manufacturer of a selected drug that is proprietary information of such manufacturer (as determined by . . . [CMS]) shall be used only by . . . [CMS] or disclosed to and used by the Comptroller General of the United States for purposes of carrying out [the Program].”²³ Seagen understands the importance of protecting confidentiality and asks CMS to honor similar protections of proprietary information submitted by manufacturers to the Agency during the course of negotiation. This is consistent with the approach taken

²¹ Initial Guidance at 55.

²² See *Bracco Diagnostics*, 963 F. Supp. at 27–28.

²³ *Id.* § 1193(c).

in other areas of federal law and policy, which have long given special consideration to such highly sensitive information.

We appreciate CMS's confirmation that the protections under FOIA, including the prohibition on disclosure of information designated as confidential without providing a pre-disclosure notification and an opportunity to raise objections to disclosure,²⁴ will apply to information submitted under the program.²⁵ We seek confirmation that the protections under government price reporting law and policy will also apply. Related, the 340B Drug Pricing Program (340B Program) generally prohibits disclosures of information submitted by manufacturers under the program.²⁶ Where confidential commercial information is protected against disclosure under this or other federal programs, CMS should follow existing precedent by protecting such information against disclosure.

V. MFP-Setting for Critically Important Products, Like Those that Treat Cancer

A. Seagen encourages CMS to set MFPs responsibly and should recognize the importance of differentiated evaluations in critical disease states, like cancer.

CMS proposes to identify a single price for use during the negotiation process based on a 30-day equivalent supply. This is unreasonable in complex disease states, like cancer. Cancer patient populations are unique and because of the nuances of disease progression, CMS must not lump therapies into buckets based solely on site of the tumor. A treatment that works well for a breast cancer patient with a HER2 mutation, for example, may be completely ineffective for a patient without such mutation. Therefore, CMS must consider only appropriate treatments for a given indication together, without bucketing treatments into oversimplified groups. This is one of the complexities leading Seagen to request different treatment for oncology therapies.

B. CMS must acknowledge that medications treating cancer, including cancer therapies treating multiple indications cannot have therapeutic alternatives in most cases, and therefore, must always be assigned the MFP ceiling.

Cancer therapies often have more than one indication, allowing them to serve multiple distinct patient populations. Because cancer patient populations can be small and heterogeneous, ongoing clinical trials of proven medications are the most efficient and expedient way to bring appropriate care to patients battling diverse cancer diagnoses. In fact, it is often the case that innovative cancer medications do not have a true

²⁴ See 45 C.F.R. §§ 5.41, 5.42.

²⁵ Initial Guidance at 29.

²⁶ Health Res. & Servs. Admin., General Instructions for Completing the Pharmaceutical Pricing Agreement 7 (2019), available at www.hrsa.gov/sites/default/files/hrsa/opa/pharmaceutical-pricing-agreement-example.pdf.

therapeutic alternative due to the specific patient population or biomarker targeted. Cancer patients require these hyper-targeted approaches to fight aggressive diseases. Therefore, Seagen does not believe CMS should start at an ASP of therapeutic alternatives unless said alternative is for the exact same indications and patient sub-populations. Within the statutory limitations, Seagen strongly encourages CMS to assign the MFP for all cancer medications with multiple indications at the statutory ceiling at initial and all renegotiations. Application of the MFP ceiling may still risk decline in investment into multiple indications.

As stated initially, while this proposed guidance is intended for the negotiation of Part D drugs for 2026 only, for the reasons outlined above there needs to be a separate opportunity to comment on the Program for Part B drugs beginning 2028.

VI. Conclusion

As a global biotechnology company, Seagen recognizes the responsibility to improve and expand access to our medicines to patients in need. Seagen appreciates the complexity of implementing a program this size and we reiterate our request that the Agency engage in thorough review and consideration of these comments. We look forward to ongoing discussions and additional opportunity to provide feedback on future IPAYs, particularly when physician administered drugs are included.

Sincerely,

A handwritten signature in black ink, appearing to read 'Sydney Abbott Osborne'.

Sydney Abbott Osborne, JD

Global Value Access Healthcare & Reimbursement Policy and Advocacy



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April 14, 2023

Submitted via Electronic Filing: IRARebateandNegotiation@cms.hhs.gov

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attn: PO Box 8016

Re: Sections 40.4 and 90.2: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Dr. Seshamani:

The Senior Care Pharmacy Coalition (“SCPC”) appreciates the opportunity to provide comments on the March 15, 2023 memorandum issued by the Centers for Medicare & Medicaid Services (“CMS”), entitled *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments* (the “Draft Guidance”), and particularly Sections 40.4 (“Providing Access to the MFP”) and 90.2 (“Monitoring of Access to the MFP”) addressing how drug manufacturers may provide pharmacies with access to drugs at “maximum fair price” (MFP). Respectfully, we believe that the Draft Guidance does not properly account either for how pharmacies purchase drugs from wholesalers, or how pharmacies are reimbursed for the sale of those drugs by Part D Plans (PDPs), even in situations where the drug manufacturer provides a discount to the drug price such as in the Part D Manufacturer Coverage Gap Discount program in operation today. For that reason, **we urge CMS to significantly revise Sections 40.4 and 90.2 to simply require that manufacturers and Part D Plans afford pharmacies access to MFP prices using the same methodologies used by manufacturers, PDPs, and pharmacies today.** There is no need to build new systems – much less systems that likely will prove unworkable or unduly disruptive in the marketplace. In Appendix A, we offer specific amendments to the respective provisions in the Guidance which we believe will meet the agency’s operational goals while avoiding undue burden for pharmacies and other affected stakeholders.

SCPC is the only Washington-based organization exclusively representing the interests of long-term care (LTC) pharmacies. SCPC's membership includes 80% of all independent LTC pharmacies. Our members serve one million residents daily in skilled nursing facilities and assisted living communities across the country.¹ Given the distinct characteristics of the LTC patient population and the enhanced clinical responsibilities of LTC pharmacies, we offer unique perspectives on CMS' initiatives and proposals, particularly how Medicare Prescription Drug Benefit ("Part D") policies and requirements impact Part D enrollees with institutional level of care needs and the LTC pharmacies that serve them.

CMS correctly notes that § 1193(a)(1)(A) of the Inflation Reduction Act (IRA) requires manufacturers to afford pharmacies and other dispensers to access MFP prices. Unfortunately, the statute provides no guidance regarding implementation. It appears that CMS has imported a concept from a different section of the IRA into the provision in the Guidance pertaining to § 1193(a)(1)(A). The unrelated provision, section 1860D-14C(c)(1)(B), concerns the Part D Manufacturer Discount which requires manufacturers to ensure that a pharmacy is paid for the difference between the "negotiated price" and the "discounted price" of a Part D drug within 14 days for electronic claims and 30 days for non-electronic claims, select provisions from another section of the IRA into the Guidance related to CMS seems to have imported the 14 day requirement – but not the 30-day requirement – into § 1193(a)(1)(A) of the Guidance. We respectfully suggest that, since Congress explicitly included a retroactive reconciliation provision in § 1860D-14C(c)(1)(B) but not in § 1193(a)(1)(A), Congress did not delegate authority to the agency to mandate how manufacturers or wholesalers may reconcile the difference between a "negotiated price" and pharmacy acquisition costs retroactively. Although the existing coverage gap discount program process operated by Palmetto² may be a useful model for reconciliation between manufacturers and Part D Plans ("PDPs" or "Plans"), Section 1193(a)(1)(A) should be implemented differently than proposed in the Draft Guidance.

The Draft Guidance misapprehends how pharmacies acquire and dispense medications. Section 40.4 suggests that manufacturers should ensure that either: (1) the pharmacy acquisition cost for a drug subject to price negotiation is at the MFP price; or (2) retrospectively, through wholesalers, as suggested in Section 90.2, reconcile the price with the pharmacy. Neither option is viable for pharmacies.

The first option for pharmacies to acquire at the MFP price is not possible to implement as pharmacies do not and cannot acquire drugs at the MFP price. Virtually all pharmacy purchases from wholesalers are at Wholesale Acquisition Cost (WAC). At the time that pharmacies purchase drugs from wholesalers, they do not know the patients to whom the drugs will be dispensed. Pharmacies in general, and LTC pharmacies in particular, do not maintain separate inventories for each of various payers that may reimburse them for dispensing a drug. Pharmacies simply do not

¹ This figure is based on pre-pandemic facility occupancy rates. Our members also serve an increasing number of individuals with LTC needs, including Medicare beneficiaries, living in community settings and at home.

² <https://tpadministrator.com/internet/tpaw3.nsf/T/CGDP%20Reconciliation>

maintain separate inventories for Part D, Medicaid, VA, DoD, Commercial, and other payers, and there are not different acquisition costs from wholesalers depending on the patient that the pharmacy anticipates will in the future be dispensed the product. Thus, there is no way for either manufacturers or pharmacies to create a special pharmacy acquisition cost at the MFP price exclusively for eligible Part D beneficiaries. The first option in the Draft Guidance – requiring the manufacturer to ensure that the pharmacy acquires the drug at the MFP price – would be impossible to implement.

Similarly, the second option - reconciliation between manufacturers and pharmacies directly or through wholesalers – is not viable. Pharmacies acquire drugs from wholesalers at WAC, and then are reimbursed by the relevant plan or payer based upon a contractual formula [often calculated based upon a published “Average Wholesale Price” (AWP)] which is intended in part to cover the acquisition cost amount. It is common that the relevant plan or payer (including Medicare Part D Plans) will dictate the price the pharmacy must charge the insured (including the Part D beneficiary). The payer-determined price pharmacies must charge typically is lower than the WAC or the contractual AWP price. To the extent that this occurs (and it is very common that the price at the point of sale is lower than the pharmacy acquisition cost), the plan or payer pays the pharmacy the AWP contractual formulary rate, and then reconciles that payment with the manufacturer, directly or through a third-party administrator, through a rebate, discount, or other mechanism. This is how the Part D program operates today, and how it should continue to operate, even for drugs with MFP prices.

Importantly, in both the Part D program (including the existing Coverage Gap Discount Program which faces similar issues) and all other programs today *the manufacturer does not reconcile the price with the pharmacy, either directly or through wholesalers*. In fact, wholesalers are not part of this information flow at all, given that wholesalers never have claims-level data about which patients received a given drug or what the applicable price should be for any given plan or payer. Instead, **any “reconciliation” of the pharmacy purchase price and the “negotiated price” takes place between the Plan and the manufacturer without pharmacy involvement**. The Draft Guidance would necessitate creation of a new mechanism relying in significant part on wholesalers, companies which lack the information necessary to undertake the intended reconciliation, and on pharmacies, which lack the time and resources necessary to engage directly with manufacturers as contemplated in the Draft Guidance. This approach, moreover, would be duplicative of a process already in place between manufacturers and PDPs that is working effectively in the Part D program today. For these reasons, we urge CMS to eliminate any suggestion or requirement that manufacturers reconcile prices directly with pharmacies or use wholesalers to do so.

We urge that CMS revise the Draft Guidance to permit manufacturers, PDPs, and pharmacies to adapt existing mechanisms to ensure pharmacy access to MFP prices. Section 90.2 of the Draft Guidance recognizes that “there is widespread use of chargeback payments and rebate mechanisms among the pharmaceutical stakeholders in the private sector, which allows for entities to receive rebates or discounts on their purchases after those purchases are made, based on the specific

population to whom the drug or biological is dispensed. As appropriate, the private sector may make modifications to these existing mechanisms to effectuate access to the MFP. SCPC urges that CMS need say nothing else in either Section 40.4 or in Section 90.2 regarding the manner in which manufacturers must comply with the statutory requirement to provide the MFP price to pharmacies or beneficiaries. This approach would allow manufacturers and PDPs to rely on existing processes without creating a duplicative process solely for MFP prices, asking wholesalers to undertake tasks for which they lack adequate information, and unduly burden pharmacies which can ill-afford the added costs and administrative burdens the provisions of the Draft Guidance would require. If the Guidance says more, we urge CMS to adopt the existing Coverage Gap Discount Program methodology, operated by Palmetto today, which allows Plans to pay pharmacies for drug acquisition cost and then has manufacturers reconcile payments to account for drug pricing discounts without the involvement of the pharmacy.

To simplify the Guidance and consistent with the comments above, we have attached a “redline” of the Draft Guidance translating our comments into specific revisions to the Draft Guidance, which we believe will result in a more streamlined and workable method for assuring that pharmacies have access to MFP pricing without undue burden.

We raise two other issues: first, the shift in drug pricing risks significant economic ripple effects across wholesalers, Plans and PBMs, Pharmacy Services Administrative Organizations (PSAOs) and others in the distribution chain. We urge CMS to clarify in the Guidance that Plans need to maintain pharmacy reimbursement to ensure that it is sufficient to cover the pharmacy’s acquisition costs and the costs of dispensing the medication, including the additional costs associated with long-term care pharmacy dispensing. Without such clarification, CMS risks damaging the existing national network of LTC pharmacies and putting patient access at risk.

Second, SCPC notes that the draft Guidance proposes to calculate the MFP price based upon the lowest unit of drug or biological, aggregating numerous drugs or biologicals with different active ingredients, different dosage forms, different strengths, and other differences. We note that this approach seems inconsistent with Congressional intent because it mixes and matches different products and different manufacturers when determining MFP. We caution that whatever pricing metric CMS chooses must be translated back to a price per NDC-11 (the specific National Drug Code the FDA assigns to each drug, specific to dosage form and strength), which is a legal prerequisite for pharmacies to process claims. The entire pharmacy electronic transaction system is based upon tracking products based upon their NDC-11, and the only way in which pharmacies will be able to offer MFP prices to beneficiaries at the point of sale is if there is price per NDC, at the NDC-11 level. We urge CMS to take this into account in updating and revising its Draft Guidance.

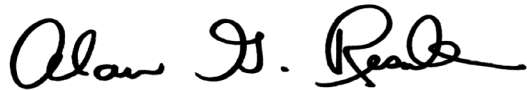
Meena Seshamani, M.D., Ph.D.

April 14, 2023

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Thank you for your consideration. If you have questions or wish to discuss our comments, please feel free to contact me at arosenbloom@seniorcarepharmacies.org or (717) 503-0516.

Respectfully submitted,

A handwritten signature in black ink, reading "Alan G. Rosenbloom". The signature is fluid and cursive, with the first name "Alan" being the most prominent.

Alan G. Rosenbloom
President & CEO
Senior Care Pharmacy Coalition

Attachment

APPENDIX A – PROPOSED AMENDMENTS TO DRAFT GUIDANCE

Section 40.4

40.4 Providing Access to the MFP

After entering in an Agreement with CMS and in accordance with section 1193(a) of the Act, the manufacturer of a selected drug that is a covered Part D drug (as defined in section 1860D-2(e) of the Act) must provide access to the MFP to MFP-eligible individuals (defined in section 1191(c)(2)(A) of the Act and section 80 of this memorandum) and to pharmacies, mail order services, and other dispensers with respect to such MFP-eligible individuals who are dispensed that drug during a price applicability period.

Under section 1860D-2(d)(1)(D) of the Act, as amended by section 11001(b) of the IRA, the negotiated prices used in payment by each Part D plan sponsor for each selected Part D drug must not exceed the applicable MFP plus any dispensing fees for such drug. In Part D, the negotiated price of a Part D drug is the basis for determining beneficiary cost-sharing and for benefit administration at the point of sale. Therefore, the requirement that the price used for beneficiary cost-sharing and benefit administration cannot exceed the MFP (plus dispensing fees) ensures that Part D MFP-eligible individuals will have access to the MFP at the point of sale. Therefore, while section 1193(a)(1)(A) of the Act specifies that manufacturers must provide access to the MFP to MFP-eligible individuals, as a practical matter that will be accomplished by Part D plan sponsors without additional steps required of the manufacturer.

However, section 1193(a)(1)(A) of the Act also requires that manufacturers provide access to the MFP for selected drugs to pharmacies, mail order services, and other dispensers with respect to MFP-eligible individuals who are dispensed such drugs. CMS intends to require that the Primary Manufacturer ensure that entities that dispense drugs to MFP-eligible individuals, including pharmacies, mail order services, and other dispensers, have access to the MFP for the selected drug in accordance with section 1193(a) of the Act and as further discussed in section 90.2 of this memorandum. ~~CMS intends to define “providing access to the MFP” as ensuring that the amount paid by the dispensing entity for the selected drug is no greater than the MFP.~~

~~CMS intends to require that Primary Manufacturers provide access to the MFP in one of two ways: (1) ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP; or (2) providing retrospective reimbursement for the difference between the dispensing entity’s acquisition cost and the MFP. As part of this obligation, the Primary Manufacturer must ensure the MFP is made available to pharmacies, mail order services, and other dispensers for units of the selected drug for which there is a Secondary Manufacturer.~~

~~Further, CMS intends to require that a Primary Manufacturer achieve certain outcomes to comply with the requirement under section 1193(a)(1)(A) of the Act to provide access to the MFP:~~

~~1. A Primary Manufacturer would be required to submit its process for making the MFP available for the selected drug in writing to CMS at least 30 days before the start of the initial price applicability year for the selected drug. CMS intends to publish these processes on the CMS IRA website. For initial price applicability year 2026, a Primary Manufacturer of a selected drug must send its process for ensuring MFP availability to CMS in writing by December 2, 2025. A Primary~~

~~Manufacturer would also be required to notify CMS of any changes to its process for making the MFP available at least 30 days before the change goes into effect.~~

~~2. CMS intends to monitor for compliance and audit, as needed, to ensure that the MFP is being made available for the selected drug. A Primary Manufacturer would be required to retain for at least ten years from the date of sale any records relating to sales of the selected drug to entities that dispense the selected drug to MFP-eligible individuals, including pharmacies, mail order services, and other dispensers for units of selected drug. See section 90.2 of this memorandum for additional details.~~

~~3. CMS intends to require that a Primary Manufacturer ensure that pharmacies, mail order services, and other dispensers as well as intermediate entities, such as wholesalers, as applicable, are reimbursed timely for the full amount of the difference between their acquisition cost for the selected drug and the MFP within 14 days. Manufacturers or their contracted entities shall not charge any transaction fee for this process. CMS intends that the Agreement would not restrict the Primary Manufacturer or Secondary Manufacturer(s) from offering a price lower than the MFP. CMS reiterates that Primary Manufacturers would be responsible for ensuring that the MFP is made available to pharmacies, mail order services, and other dispensers that dispense the selected drug to MFP-eligible individuals, including ensuring that MFP is available for units of the selected drug for which there is a Secondary Manufacturer.~~

Section 90.2

90.2 Monitoring of Access to the MFP

In accordance with section 1193(a)(3)(A) of the Act, under the Agreement with CMS with respect to a price applicability period, access to the MFP with respect to such a selected drug shall be provided by the Primary Manufacturer to MFP-eligible individuals at the pharmacy, mail order service, or other dispenser at the point of sale, and to the pharmacy, mail order service, or other dispenser with respect to such MFP-eligible individuals who are dispensed the selected drug. Existing systems under the Coverage Gap Discount Program exist for manufacturers and Plans to address these issues and these systems should be used in the future to ensure pharmacies are appropriately reimbursed by Plans so that MFP-eligible beneficiaries maintain access to MFP prices without harming the pharmacy.

~~Further, in accordance with section 1193(a)(5) of the Act, which requires that the manufacturer comply with requirements determined by the Secretary to be necessary for purposes of administering the program and monitoring compliance with the program, and section 40.4 of this memorandum, CMS intends to require that the Primary Manufacturer establish safeguards to ensure the MFP is available to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers on units of the selected drug for which there are Secondary Manufacturers, as described in section 40.4 of this memorandum. CMS reiterates that the requirement to provide~~

~~access to the MFP applies to all sales of the selected drug to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers that are providing a selected drug to an MFP-eligible individual, as discussed in section 80 of this memorandum.~~

~~Moreover, in accordance with section 1196(a)(3)(A) of the Act, CMS intends to establish procedures for reporting violations related to access to the MFP with respect to MFP-eligible individuals who are enrolled in a PDP under Part D of title XVIII or MA-PD plan under Part C, as described later in this section.~~

Each component of the pharmaceutical supply chain may have a role in making the MFP available to MFP-eligible individuals, but it is ultimately the Primary Manufacturer's responsibility to ensure access to the MFP. There are various methods by which dispensing entities and MFP-eligible individuals can determine whether they are accessing the MFP for a selected drug.

For example, under section 1195(a) of the Act, the MFPs for selected drugs will be published by CMS, giving the public and other interested parties an opportunity to know the MFP for each selected drug, as well as the explanation for each MFP (see section 60.6 of memorandum for additional details). Under section 1191(d)(1), the MFPs for selected drugs for initial price applicability year 2026 must be published by September 1, 2024. In addition, CMS anticipates that pharmaceutical database companies will publish the MFPs such that they would become more readily accessible to pharmaceutical purchasers. CMS believes such transparency of the MFPs for selected drugs will help dispensing entities and MFP-eligible individuals to know the MFP for a selected drug and determine whether they are able to access the MFP. CMS is seeking comments on additional ways that CMS could help dispensing entities and MFP-eligible individuals know the MFP for a selected drug and determine whether they are able to access it.

Moreover, with respect to operationalizing access to the MFP, CMS intends to leverage existing mechanisms to ensure that dispensing entities have access to the MFP, and that the MFP for a selected drug is provided only to MFP-eligible individuals. ~~For example, each Medicare Part D plan is required to use a unique Part D processor identification number (RxBIN) and Part D processor control number (RxPCN) combination to identify a Medicare Part D payer. This existing mechanism will ensure that the pharmacy is able to identify at the point of sale whether the individual is an MFP-eligible individual.~~

In addition, there is widespread use of chargeback payments and rebate mechanisms among the pharmaceutical stakeholders in the private sector, which allows for entities to receive rebates or discounts on their purchases after those purchases are made, based on the specific population to whom the drug or biological is dispensed. As appropriate, the private sector may make modifications to these existing mechanisms to effectuate access to the MFP.

~~For example, a pharmacy may purchase a medication for \$100 per bottle and the MFP as applied to this selected package is \$80. The Medicare beneficiary is enrolled in a Part D plan under which coverage of the selected drug is available, thus the beneficiary is an MFP-eligible individual. For this example, the plan has not negotiated a lower price for the medication. The pharmacy provides the negotiated price (i.e., MFP plus a dispensing fee) at the point of sale to the Medicare beneficiary. As a result of this transaction, the pharmacy is owed \$20 by the manufacturer. The~~

pharmacy would submit the information regarding the \$20 chargeback amount to its wholesaler and receive a credit from the wholesaler for that amount. The wholesaler would be compensated by the manufacturer after billing the manufacturer for the chargeback amount.



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VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
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Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Sionna Therapeutics appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

Sionna Therapeutics is a life sciences company dedicated to developing highly effective and differentiated treatments for cystic fibrosis (CF) by normalizing the function of CFTR, the key protein associated with disease progression in CF. Building on over a decade of extensive research on the genetic mutations associated with CF and founded in 2019, Sionna is advancing a pipeline of small molecules engineered to correct the protein defects caused by $\Delta F508$, the most common mutation that affects the CFTR protein. The company has a first-in-class portfolio of programs targeting correction of NBD1, the key and unique mechanism to enable full restoration of $\Delta F508$ -CFTR function, and complementary programs targeting ICL4 and TMD1. Sionna's pipeline has the potential to deliver best-in-class efficacy and reach previously unachievable levels of long-term benefit for people with CF.

In addition to being a company focused on improving the standard of care for people living with cystic fibrosis, we are a group of individuals who collectively have contributed hundreds of years supporting the research and development of biopharmaceuticals. Our passion and dedication to drug development drives a priority to ensure that no modality of treatment, for example small molecules, or group of patients, for example those of Medicare eligibility, are at a disadvantage to the continued investment and development of therapeutic advancements. We have serious concerns about the Inflation Reduction Act and the broad implications it will have on future investment, drug development and ultimately improved standards of care for Americans.

For example, the nine years of pre-negotiation exclusivity afforded to small molecule therapeutics may in many cases be insufficient to attract investment necessary to undertake highly risky R&D in CF and other indications. This will skew investor interest toward large molecule modalities that are difficult to genericize and thus generate less long-term societal value. It will reduce investment in drugs that can reach intracellular targets. And it will dissuade companies from tackling the important challenges of treating diseases that affect America's seniors and other Medicare populations.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact Mike Cloonan, President & CEO by telephone at 617-819-2020 or by e-mail at mike.cloonan@sionnatx.com if you have any questions regarding our comments.

Sincerely,

Mike Cloonan
President & CEO
Sionna Therapeutics



April 14, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and
Director of the Center for Medicare
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Re: Comments on “Initial Guidance” for Implementation of the Medicare Drug Negotiation Program Established by IRA

Dear Deputy Administrator Dr. Meena Seshamni,

On behalf of the Small Business & Entrepreneurship Council (SBE Council), I write to express concern about the initial implementation guidance for the Medicare Drug Price Negotiation Program established by the Inflation Reduction Act (IRA). This guidance proposed by the Centers for Medicare & Medicaid Services (CMS) would pose new impediments to the research and development of life-saving drugs, imperiling patients and small biotechs.

SBE Council is an advocacy, research and education organization dedicated to protecting small business and promoting entrepreneurship throughout the United States. Small businesses dominate every sector of the U.S. economy, which means their viability and growth is vital to quality job creation, innovation and competition within each industry. This includes the life-sciences industry, where small- and medium-sized companies employ over 70% of the nearly 1.9 million-member workforce.

These start-ups and small firms play a critical role in developing life-saving medicines, from novel cancer drugs to Covid-19 vaccines. In fact, small biotech companies developed more than half of FDA-approved drugs between 2011 and 2020.

To continue serving the needs of patients, these innovators rely on a transparent regulatory environment that actively seeks out and values their input. However, the new implementation guidance largely shuts them out of the government's decision-making process for the Price Negotiation Program.

While CMS has allowed stakeholders to submit their comments on the new guidance, they limited the comment period to just 30 days -- around half of the time normally allotted for public input on initial rules. For a large biotech company, marshaling the resources to submit comments within this narrow timeframe may not be as serious a challenge. But the same cannot be said for start-ups, who often do not have the administrative capacity to do so.

By severely constraining the ability of smaller innovators to engage with CMS on this guidance, the agency is sending a strong signal that it will not grant their input the attention it deserves.

The price-setting process, as reflected within the guidance, also severely lacks transparency. There's no guarantee that CMS will take stakeholder comments into account at all -- and respondents will have to wait 17 months before that crucial information is made available to them. That's six months *after* the maximum fair prices for relevant drugs have already been determined.

Soliciting insight from those directly involved in creating new treatments should give CMS an opportunity to hone its rules before making a final determination. Instead, the agency has opted to disengage with the life-sciences community -- particularly its smaller stakeholders.

This follows the problematic trend that began with the IRA itself. By imposing stringent price controls on a range of life-saving drugs, Congress failed to account for the devastating impact the law would have on the small- and medium-sized companies responsible for research and development.

CMS' initial guidance compounds the arbitrary nature of these policies, chilling innovation and jeopardizing patient access to new medicines. The provisions regarding "therapeutic reference pricing" and "unmet medical needs" encapsulate this problem.

The former would make price-setting decisions by referencing alternative treatment options available. Such reference pricing quickly breaks down in practice because of ill-defined standards. Even ostensibly minor differences between two "similar" medicines can have major clinical implications for patients. Because no two people living with a disease are exactly alike, some may respond well to one therapeutic but not another. By relying on therapeutic reference pricing, CMS would overlook patients' needs and inappropriately value new treatments that may be their best option for staying healthy.

Similar concerns apply to the agency's rule regarding drugs that address unmet needs. CMS has stipulated that it may adjust the price-setting starting point for treatments geared towards unmet medical need, which the agency defined as "treating a disease or condition in cases where very limited or no other treatment options exist." But this definition is so narrow in focus that it could exclude *any* medicine that provides patients with a measurable clinical benefit from the exemption criteria, provided it is not the only one that does so. Cutting-edge drugs that treat life-threatening diseases will be systematically devalued, and patients will bear the brunt.

In the long-term, provisions like these undermine the research and development ecosystem that enables new drugs to reach patients in the first place. If CMS aggressively imposes price controls in an arbitrary fashion, start-ups and investors in small biotechs will lose confidence that they can make a sufficient return on investment.

This is already happening in response to the IRA. Last October, the small biotech firm Alnylam Pharmaceuticals announced that they were suspending development on a treatment for a rare genetic eye disease, citing the law as their impetus for doing so.

These harmful consequences are only exacerbated by the guidance rules concerning intellectual property - which undergirds all innovation - and the emerging biosimilars market.

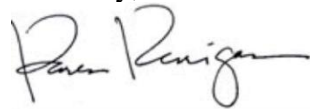
The guidance notes that CMS "intends to consider the length of...available patents and exclusivities" in deciding whether to force down the price of a drug. But this is a non-starter for small biotech companies. It commonly costs \$2 billion to bring a new treatment to market, a process that can span a decade. Acquiring exclusive rights to the drug is the *only* way to guarantee a return on investment.

The impact will be particularly damaging for research and development that happens after a drug receives FDA approval. Manufacturers often seek additional patents so they can fine-tune their drugs and bolster efficacy. Post-approval research is especially crucial for cancer drugs. As one example, Merck's cutting-edge melanoma immunotherapy drug Keytruda is only halfway through its full development program.

Small biotechs producing biosimilars will face similar obstacles that hinder development. While the IRA enables biosimilar developers to request a delay on price controls for specific drugs, CMS will not make this option available to those currently involved in litigation against reference manufacturers. But these legal disputes often precede the given biosimilar gaining approval and coming to market within the necessary time period.

Small- and medium-sized companies are already buckling under existing IRA provisions that encumber research and development. For the sake of those who develop life-saving treatments, we strongly urge CMS to correct the provisions of their implementation guidance that will intensify this crisis.

Sincerely,



Karen Kerrigan
President and CEO

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Protecting Small Business, Promoting Entrepreneurship



13 April 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
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IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure,

Sparrow Pharmaceuticals appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program Guidance Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comment posted on the CMS website on 15 March 2023 (Drug Price Negotiation Program Guidance).

Sparrow is a private, clinical-stage pharmaceutical company that aims to spare patients the ravages of steroids. We have two small molecule drugs in ongoing Phase 2 clinical trials.

- SPI-47 is a glucocorticoid. Millions of US patients rely on glucocorticoid medications (e.g., prednisone, dexamethasone) to control autoimmune diseases, prevent transplanted organ rejection, and treat various cancers, severe COVID disease, and other conditions. But they do so at tremendous costs: glucocorticoids are associated with ~10% of all drug adverse events reported to FDA and ~10% of all drug-related hospitalizations in the US. SPI-47 will be a combination of prednisolone (a glucocorticoid) with a novel small molecule drug (SPI-62) that modulates glucocorticoid metabolism in a manner that has potential to prevent or reverse many glucocorticoid adverse events whilst maintaining glucocorticoid efficacy.
- SPI-62 as monotherapy has potential to prevent or reverse the morbidity associated with cortisol (our natural glucocorticoid) excess caused by benign tumors: Cushing's syndrome (an orphan disease) and autonomous cortisol secretion (a common but mostly undiagnosed disease).



Although Sparrow, even if successful, will not have products on the market until after 2026, the proposed guidance will be harmful to Sparrow's ability to provide innovative therapies to millions of US patients with unmet medical needs.

Recognizing that CMS is not seeking comments on Section 30, its negative impact on our business is so severe that this letter would be incomplete without elaborating our concerns.

That innovative small molecule drugs are subject to CMS price negotiation only 9 years after launch is harmful to several key Biden Administration goals. That needs to be changed to 13 years to put small molecules on equal footing with biologics, lest the industry continue a shift to fewer small molecules and more biologics, which has started already.

- The shift will increase drug and other medical costs in the long-term, exactly the opposite of IRA's intent.
 - During exclusivity, biologics are on average more expensive than small molecules.
 - Biologics are often administered by infusion, which brings additional Part B costs on top of higher Part D costs.
 - It is more complex to genericize a biologic to a biosimilar than an innovative small molecule to a generic.
 - Biosimilars are much more expensive than generics. More high-priced biosimilars will become a perpetual feature of US healthcare.
- The shift will reduce our industry's productivity to answer President Biden's "cancer moonshot".
 - Many drug targets that could be the basis for future cancer cures are inside cells, and so not accessible by biologics.
 - As companies reduce resource commitment to small molecules, some of those targets will be passed over for drug development.
 - This will impact other areas of medicine besides cancer.
- The shift will negatively impact high-quality US jobs in small molecule drug manufacturing, just as the Administration aims to expand the capacity to ensure US supply of essential medicines. Without a strong supply of innovative small molecules, that sector of US industry will be forced to contract rather than expand.

For Sparrow specifically, the small molecule penalty makes it more challenging to attract the financing essential to continue development of our innovations. Because our target is found only inside cells, it is not amenable to a biologic approach. We have a chance to deliver novel therapies that are effective, safe, convenient, and cost-effective for millions of US patients only if we can continue to attract capital to fund small molecule drug development.

Regarding Section 50.2, Sparrow respectfully requests that CMS processes for determining the Maximum Fair Price for individual medicines should account broadly for all associated value



inputs. Rather than the narrow cost-effectiveness analyses used historically by HTA bodies such as ICER, we suggest that CMS utilize generalized cost-effectiveness analyses that account for value to patients, caregivers, health care providers, and society at large.

Sparrow's SPI-47 might be exemplary of a drug with value inputs that traditional models would not capture adequately. For treatment of autoimmune diseases, SPI-47 aims to supplant two classes of current therapies.

- Glucocorticoids, as mentioned above, are associated with considerable adverse event burden which leads not only to patient morbidity, but also to additional burden on caregivers and health care providers as well as substantial healthcare costs to society. If SPI-47 works as hoped, much of that morbidity, burden, and cost will disappear.
- Immune-suppressing biologics (e.g., adalimumab) which are the highest cost drug class for both CMS and private insurers. SPI-47, if successful, will offer efficacy and safety comparable to the best biologics for multiple autoimmune and inflammatory diseases with superior convenience (once-daily pill). The more immune-suppressing biologics can be replaced with a lower-price alternative (i.e., SPI-47) the greater the savings to CMS and the US healthcare system overall.

It's important for Sparrow that CMS adopts processes that allow for less traditional value inputs such as the morbidity, burden, and cost of drug adverse effects that no longer occur and the cost of high-priced drugs that can be utilized substantially less than in the past.

Sparrow appreciates your consideration of these comments as you develop the Drug Price Negotiation Program. We look forward to continued interaction with CMS toward successful implementation of this program in a manner that minimizes the potential harm to US patients (i.e., all of us) from fewer innovative medicines such as (hopefully) SPI-47 and SPI-62. Please contact me by e-mail david@sparrowpharma.com if you have any questions regarding this letter.

Best regards,

David A. Katz, Ph.D.
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March 20, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Department of Health and Human Services
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Dr. Seshamani:

We are writing to you in our capacity as academic researchers and scientists who have studied and published extensively on the subject of patient-centered comparative effectiveness research and population health measurement. Specifically, we want to comment on Section 50.2 and 60.3.3 of your March 15, 2023 memo referenced above.

Language in the initial guidance for Medicare Price Negotiation includes restrictions on the use of the QALY to assess comparative benefit and safety of therapeutic alternatives. Your office seeks comments on “other metrics, in addition to QALYs, that may treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill and that CMS should also exclude from consideration when developing offers and reviewing counteroffers.” With this letter, we provide our input on this topic.

The concern expressed by some is that the QALY systematically discriminates against elderly, disabled or terminally ill Americans when used to inform resource allocation decisions or price determinations. **While the QALY remains controversial, placing value on both life extension and quality of life should not be.** Not all medical interventions financed through federal or state resources extend life. Interventions that improve patient quality of life without extending life are essential for countless patients and their families. For example, many of the FDA-approved treatments for patients with chronic obstructive pulmonary disease (COPD) and emphysema improve symptoms and lung function and also reduce burdensome and expensive disease exacerbations. The impact these interventions have on well-being and quality of life is substantial and important to patients and their families. Yet, there is no direct evidence that these treatments improve life expectancy. There also are treatments that improve survival but at a quality of life that is lower for patients. Failing to value improvements in quality of life might penalize such treatments in coverage and payment determinations and may limit access for patients suffering from poor quality of life.

In 2015, Professor Richard Cookson enumerated and discussed the ethical concerns and issues regarding discrimination with the QALY.¹ The U.S. National Academy of Sciences took up this issue, too.² In both reports, the authors find valid reasons for measuring both quality of life and longevity improvements but acknowledge some limitations of the QALY as a vehicle for doing so. Since these reports were completed, scientists (including five of us) have created alternatives to the QALY that retain the ability to assess and value well-being and quality of life to inform policy and resource allocation decisions without discriminating against any members of society.^{3,4,5} The equal value of Life Years Gained (evLYG), Healthy Years in Total (HYT) and the Generalized Risk Adjusted QALY (GRA-QALY) method are important advances in the field of population health measurement and comparative effectiveness research. These tools were designed specifically to mitigate the concerns about the QALY and provide a means by which population health measures can be explicitly considered as part of policy evaluations.

Importantly, in the National Disability Council's report on *"Alternatives to QALY-Based Cost-Effectiveness Analysis for Determining the Value of Prescription Drugs and Other Health Interventions,"* the Council concludes that the evLYG, "eliminates the risk of undervaluing life-extension for people with disabilities," and that the "HYT is a better approach.....because it removes the devaluation of life extension of people with disabilities."⁶ **In other words, these new metrics have overcome the concerns of disability advocates, while preserving the ability to assess quality of life alongside survival gains.**

Health care authorities in other countries (Australia, Canada, France, Germany, Japan, Netherlands, Sweden, and the UK to name a few) use the outcomes of comparative effectiveness research, including improvements in both life expectancy and quality of life, to inform their population health care funding decisions. They do so because they understand that resource allocation decisions can have positive and negative effects on population health. By using the full range of comparative effectiveness evidence on treatments, these jurisdictions consider all evidence seen as useful and equitable as well as necessary for the efficient use of scarce health sector resources. But in the U.S., we do not routinely – nor as a matter of federal policy - use comparative effectiveness research based on the QALY to inform pricing, coverage and reimbursement decisions. While we understand the QALY has certain limitations and is politically charged (H.R. 485, for example) for federal health care policy, **we suggest that CMS not restrict use of valid and non-discriminatory alternatives in their assessment of comparative clinical benefit of therapeutic alternatives.**

Dr. Seshamani, we applaud the work that has begun at CMS to implement the health care provisions of the IRA. This is very important work that will benefit Medicare beneficiaries, of which some of us now count ourselves amongst. We now have useful and valid alternatives to the QALY that allow for the assessment and valuation of treatments that improve population health without discriminating against vulnerable patient populations. Indeed, these new measurement approaches can even promote health equity by recognizing the additional value of improving health outcomes for vulnerable populations. Many Americans, including Medicare beneficiaries, continue to suffer the burden of poor quality of life. CMS should ensure that its processes and methods that incorporate comparative effectiveness research into decision

making can explicitly recognize the value of reducing this burden to improve patient outcomes by acknowledging that there are available measures that incorporate life extension and quality of life without discrimination.

We respectfully ask that CMS not exclude the evLYG, HYT and GRA-QALY metrics from the list of acceptable evidence the agency might collect and use concerning the comparative effectiveness and safety of therapeutic alternatives as part of Medicare Price Negotiation.

Sincerely,

Sean D. Sullivan, PhD¹ (sdsull@uw.edu)

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Disclaimer: The opinions expressed in this communication are the authors' and do not necessarily reflect the views of their respective institutions.



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April 14, 2023

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Attn: PO Box 8016

***Re: Medicare Drug Price Negotiation Program: Initial Memorandum,
Implementation of Sections 1191 – 1198 of the Social Security Act for
Initial Price Applicability Year 2026, and Solicitation of Comments***

Dear Dr. Seshamani:

Sunovion Pharmaceuticals Inc. (“Sunovion”) appreciates the opportunity to provide comments on the March 15, 2023, memorandum issued by the Centers for Medicare & Medicaid Services (“CMS”), entitled *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments* (the “Guidance”). We incorporate by reference the comments submitted by PhRMA and add to those comments by describing the need for CMS to carefully consider the unique attributes of medications for mental illness and other conditions affecting the central nervous system as the negotiation framework is established for 2026 and beyond, especially with respect to consideration of “Unmet Medical Need” and “Therapeutic Alternatives.”

Sunovion is a global biopharmaceutical company focused on the innovative application of science and medicine to help people with serious medical conditions. With patients at the center of everything we do, Sunovion has charted new paths to life-transforming treatments that reflect ongoing investments in research and development and unwavering commitment to support people with psychiatric and neurologic conditions.

Of particular relevance to these comments, Sunovion has researched and brought to market innovative treatments for conditions impacting the central nervous system including: (1) Latuda®, an atypical antipsychotic medication indicated for the treatment of adults and adolescents (13 to 17 years) with schizophrenia, for adults, children and teens (10 to 17 years) with depressive episodes that happen with bipolar I disorder (bipolar depression), or for use with lithium or valproate to treat adults with depressive episodes that happen with bipolar depression; and (2) Aptiom®, an anti-epilepsy medicine indicated for the treatment of partial-onset seizures in patients 4 years of age and older. We are also developing a new medication for schizophrenia, ulotaront, a TAAR-1 agonist¹. As such, we have particular insight into the medical needs of patients living with schizophrenia, bipolar disorder, and epilepsy.

Guided by our commitment to patients and our ongoing focus on developing treatments in neurology and psychiatry, Sunovion focuses these comments on the following recommendations:

- 1) CMS should consider the unique nature of mental illness as the agency works to finalize the negotiation guidance and its application to potentially selected mental health medications. CMS should conduct additional direct outreach to individuals living with mental illness and their caregivers, as well as clinical experts and industry, to appropriately shape the negotiation parameters that may be used for mental health medications.
- 2) CMS should rethink its approach to establishing therapeutic alternatives, given that mental health drugs with the same label indication and in the same therapeutic class may not be therapeutically interchangeable.
- 3) CMS should clarify and expand upon its definition of unmet need to better recognize the significant outstanding unmet needs of people living with mental illness.
- 4) CMS should ensure continued broad formulary access to mental health medications.

CMS Should Consider the Unique Nature of Mental Illness and the Challenges of Developing Treatments

Sunovion is among only a few companies focused on developing treatments for serious mental illness (SMI), thus we are particularly concerned that the final Guidance must appropriately account for the unique nature of mental health medications, and

¹ [Heffernan, et al., Ulotaront: A TAAR1 Agonist for the Treatment of Schizophrenia;](https://pubmed.ncbi.nlm.nih.gov/35047111/)
<https://pubmed.ncbi.nlm.nih.gov/35047111/>

acknowledge that drugs within these unique therapeutic classes are not interchangeable. The draft Guidance, without considering the importance of mental health medications and their lack of interchangeability or substitution, risks inappropriate evaluation of these important treatments.

Almost 30% of Medicare beneficiaries live with mental health conditions. As recently reported by the Commonwealth Fund:²

[a]bout one in four Medicare beneficiaries live with mental illness — conditions such as depression, anxiety, schizophrenia, and bipolar disorder — but only 40 percent to 50 percent receive treatment. The prevalence of mental illness is about equal among beneficiaries enrolled in traditional Medicare (31%) and those in Medicare Advantage plans (28%), although variation in data sources and measurement make comparisons difficult.

Mental illness is experienced most by those beneficiaries under age 65 who qualify for Medicare via disability, as well as by low-income beneficiaries dually eligible for Medicare and Medicaid. It is also more pervasive in beneficiaries from American Indian/Alaska Native and Hispanic communities relative to other racial and ethnic groups.

An estimated 14.2 million adults in the United States live with one or more serious mental illnesses such as schizophrenia or bipolar disorder.³

Schizophrenia and related psychotic disorders affect up to 2.1 million Americans and an estimated 43% of insured people with schizophrenia are covered by Medicare.^{4,5} “annual healthcare costs exceed \$155 billion. People living with schizophrenia often experience a reduced quality of life (QOL) and are more likely to be homeless, unemployed, or living in poverty compared with the general population. Life expectancy for patients with schizophrenia is 15 to 20 years below the average and is complicated by numerous comorbidities, such as weight gain, increased cardiovascular risk, and

² Medicare’s Mental Health Coverage: What’s Included, What’s Changed, and What Gaps Remain (March 2, 2023), available at <https://www.commonwealthfund.org/publications/explainer/2023/mar/medicare-mental-health-coverage-included-changed-gaps-remain> (references omitted).

³ Geils, Incentivizing Drug Development in Serious Mental Illness, *Clin Ther.* 2022 Sep;44(9):1258-1267. doi: 10.1016/j.clinthera.2022.08.002.

⁴ <https://www.nimh.nih.gov/health/statistics/schizophrenia>

⁵ <https://www.umass.edu/public-health-sciences/news/more-adults-schizophrenia-have-insurance>

changes in mood and cognition. Treatment nonadherence can increase the risk of relapse, rehospitalization, and self-harm, leading to a reduced QOL and increased economic burden.”⁶

Bipolar disorder is also prevalent within the Medicare community. The disease is estimated to affect 2.8% of the population, although that is widely understood to be underestimated due to diagnosis delays. Those with the disease experience greater hospitalization, increased direct healthcare costs, and significantly increased economic and humanistic costs. Direct increased healthcare costs are estimated at \$20,846 per patient per year.⁷

While the needs for better access to mental health services and novel treatments continue to grow, challenges to develop new medicines that better meet the needs of patients are significant. Consider these key findings from a recent review by the Tufts Center for Evaluation of Value and Research on drug development in SMI:

Clinical development timelines for drugs used to treat severe mental illness are some of the longest. The FDA approval process is 38% longer for central nervous system (CNS) versus non-CNS drugs. When CNS drugs fail, they tend to do so in late-stage trials and after significant financial investment.

Clinical trial success rates are low; 6.2% of drugs for the CNS that enter into clinical trials, including drugs for serious mental illness, achieve market approval (versus 13.3% for non-CNS drugs).

Serious mental illness is a particularly difficult area to conduct clinical research in, especially in regards to recruitment and retention in trials. Individuals may have difficulty accepting their diagnosis and initiating treatment and be less willing to seek participation in clinical trials.⁸

Given the scale of the mental health crisis, the Administration has repeatedly called out the importance of access to treatment. For example, in his May 1, 2022 Presidential Proclamation for National Mental Health Awareness Month, President Biden emphasized that “less than half of Americans struggling with mental illness receive the

⁶ Economic Impact of Schizophrenia, *Am J Manag Care*. 2020;26:S62-S68. <https://doi.org/10.37765/ajmc.2020.43013>.

⁷ Dembek, C., Mackie, d., Modi, K. et al. The economic and humanistic burden of bipolar disorder in adults in the United States. *Ann Gen Psychiatry* 22, 13 (2023). <https://doi.org/10.1186/s12991-023-00440-7>

⁸ Geils, *supra*.

treatment they need — even fewer within Black and Brown communities.”⁹ Secretary Becerra and several other leaders in the Administration echoed these sentiments.¹⁰ It is paramount that newly established Administration policies, including the drug price negotiation framework, do not serve to undermine broader goals related to treatment access and the importance of developing new treatments that may improve health and functional outcomes for individuals living with mental illness.

CMS Should Rethink its Approach to Therapeutic Alternatives for Mental Health Medications Due to Lack of Interchangeability

Section 1194(e)(2) of the IRA requires CMS to consider evidence of alternative treatments to a select drug in evaluating the drug’s value for purposes of price negotiation. The draft Guidance, in section 50.2., repeats the four elements in the statute that the Agency must consider in evaluating “evidence about therapeutic alternatives”:

1. The extent to which the selected drug represents a therapeutic advance compared to existing therapeutic alternatives for the selected drug and the costs of such existing therapeutic alternatives;
2. FDA-approved prescribing information for the selected drug and its therapeutic alternatives;
3. Comparative effectiveness of the selected drug and its therapeutic alternatives, including the effects of the selected drug and its therapeutic alternatives on specific populations (including individuals with disabilities, the elderly, the terminally ill, children, and other patient populations, herein referred to as “specific populations”); and
4. The extent to which the selected drug and the therapeutic alternatives to the drug address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy.

Mental health drugs are not therapeutically equivalent, even when indicated for the same disease or within the same therapeutic class. CMS’ proposed use of therapeutic

⁹ <https://www.whitehouse.gov/briefing-room/presidential-actions/2022/04/29/a-proclamation-on-national-mental-health-awareness-month-2022/>

¹⁰ <https://www.hhs.gov/about/news/2022/05/03/secretary-becerra-and-hhs-leaders-recognize-mental-health-awareness-month-2022.html>

alternatives is of particular concern for mental health medications, where it may be difficult or impossible to identify a true therapeutic alternative due to the lack of interchangeability within these classes. Clinicians and researchers continue earnest efforts to understand the complexities of mental health and brain function, but physicians remain limited in their ability to know how different patients will react to available treatments.¹¹ As explained by a prominent mental health physician and researcher:

[T]he treatment of mental illness is almost always ‘trial and error,’ and in many instances requires long-term treatment. In fact, the available published evidence suggests that only 25 percent to 33 percent of people who have a mental disorder experience a complete clinical response to the first two to three medications, even when prescribed in the presence of ongoing psychotherapy.¹²

The Tufts CEVR Report on drug development in SMI also found that “[f]inding an effective and tolerable treatment regimen for serious mental illness is complicated by its heterogeneity and complex biology. In any year, approximately 40% of individuals with schizophrenia, 50% of individuals with bipolar disorder, and 35% of individuals with major depression remain untreated.”¹³ Another study estimating Part D’s impact on medication access among Medicare/Medicaid dual eligible beneficiaries “found that 30.2% of antidepressant users, 23.7% of antipsychotic users, and 12.3% of mood stabilizer users had used more than one drug in the class in 2002.”¹⁴ Numerous other studies have documented the same issues.¹⁵

In clarifying the statutory criteria, the draft Guidance suggests that CMS will examine peer reviewed clinical trial and other studies, both to evaluate whether the select drug constitutes a “therapeutic advance” over “therapeutic alternatives” and serves an “unmet medical need.” We respectfully submit that the draft Guidance is insufficient and inadequate, as there are several classes of drugs, including mental health drug

¹¹ See Geils, *supra* (noting that research and development of serious mental illness medications is limited by the lack of information regarding “the inherent complexity of the brain” and the “limited knowledge of neuropathways.”)

¹² Joseph R. Calabrese, M.D., “Why I’m Speaking Out Against the Proposed Medicare Part D Change—And Why You Should, Too” (Feb. 4, 2014) (emphasis in original), available at <http://careforyourmind.org/why-im-speaking-out-against-the-proposed-medicare-part-d-change-and-why-you-should-too/>.

¹³ Geils, *supra*.

¹⁴ Julie Marie Donohue & Richard Gabriel Frank, Estimating Medicare Part D’s Impact on Medication Access Among Dually Eligible Beneficiaries with Mental Disorders, *Psychiatric Servs.* 58:10 (2007), at 1285-1291.

¹⁵ Geils, *supra*.

classes, for which the literature is unlikely to accurately depict the extent to which a select drug in a therapeutic class is not substitutable or an alternative to other drugs with an indication for the same disease.

One of the criteria that CMS in the draft Guidance proposes to adopt is the consideration of “health outcomes, intermediate outcomes, surrogate endpoints, patient-reported outcomes, and patient experience.” However, at least in the mental health space, some of these measures do not exist. For example, there are few relevant “intermediate outcomes” and challenging “surrogate endpoints” by which to measure mental health drugs.¹⁶ Thus, many of the proposed criteria suggested by CMS will not be helpful in its evaluation of alternatives. We call on CMS to recognize that a “one-size fits all” approach to the assessment of drugs in different therapeutic classes is not appropriate and will significantly disadvantage certain classes of medications, and discourage development of novel medications in areas of significant unmet need.

CMS does state that “[h]ealth outcomes such as changes in symptoms or other factors that are of importance to a person, and patient-reported outcomes would also be considered. CMS intends to focus the review of clinical benefit on outcomes of particular importance to the condition or disease being treated by the selected drug and will determine such outcomes from the CMS-led literature review and information submitted by manufacturers and the public through the Negotiation Data Elements ICR, described in section 50 of this memorandum.” Draft Guidance 62.3.3.1. Unfortunately, however, many of the factors that are of importance to a person, such as side effects that are notoriously difficult to manage, are not fully addressed in the literature, and will never be captured in a “literature review.” We urge the Agency to be more refined in its analysis and to consider a broader set of relevant materials beyond what is in the literature.

Finally, the proposed CMS analysis will likely conflict with the Food, Drug and Cosmetic Act and the Public Health Services Act. For example, the guidance states that CMS intends to consider whether the product “represents a therapeutic advance compared to existing therapeutic alternatives” and whether it fills an “unmet medical need”—but these determinations are highly detailed scientific inquiries undertaken by teams of scientists at the FDA—CMS has neither the staff nor resources to be able to conduct these reviews, and reading the published scientific literature will not inform the Agency as to whether actual therapeutic advances exist. (For example, a review of published

¹⁶ Geils, *supra* (noting that accelerated approval is valuable to manufacturers generally, but that “it is useless in disease areas without established surrogate or intermediate end points, such as SMI [serious mental illness]”).

studies regarding any particular mental health medication likely would turn up few, if any, of the peer-reviewed studies and reports identified above.)

While we acknowledge that the draft Guidance includes a glancing reference to the patient and caregiver perspective, it does not appear that CMS will adequately consider these important voices, much less take the time to appreciate the unique ways in which mental health medications serve these communities. For that reason, we urge CMS to meet with potentially affected stakeholders including patients, caregivers, and physician experts to provide additional future comment opportunities regarding the most appropriate way to identify comparators for mental health medications selected for negotiation. We also urge CMS to develop a more comprehensive process for consideration of “therapeutic alternatives” that permits drug sponsors, who often have the most comprehensive information about their products and potential alternatives, to identify proposed therapeutic alternatives or the lack thereof.

CMS Must Clarify and Expand Upon the Definition of “Unmet Medical Need” to Recognize the Significant and Ongoing Unmet Needs of Individuals with Mental Illness

Another of the four criteria identified in Section 1194(e)(2)(C) of the Act, and carried over into the draft Guidance, is “the extent to which the selected drug and the therapeutic alternatives to the drug address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy.” The draft Guidance interprets the phrase “unmet medical need” to mean “treating a disease or condition in cases where very limited or no other treatment options exist.” Draft Guidance 60.3.3.1; *see also* 60.3.3.2 (“For selected drugs with no therapeutic alternatives, CMS intends to adjust the starting point for the initial offer based on the extent to which the selected drug fills an unmet medical need.”). We respectfully submit that this definition is too broad and too simplistic, and therefore inappropriate for mental health medications.

Read literally, the draft Guidance would never consider any mental health drug subject to negotiation as addressing an “unmet medical need” as there are dozens of drugs that treat mental health today. There are “first-generation” antipsychotics like lithium and haloperidol, each of which is an “available therapy” but would rarely be a first line treatment today. A second generation of “atypical antipsychotics” consisting of numerous branded and generic medications are also available. Yet, with all these treatments, many Medicare beneficiaries *still* are unable to find a treatment that works for them. The current construct of “therapeutic alternatives” and “unmet medical need” in the draft Guidance could inappropriately lead to the comparison of innovative

second or third generation mental health treatments to older generics which may have markedly different side effect profiles and efficacy.

Instead, for the 25% of Medicare beneficiaries living with schizophrenia, bipolar disease, or other mental health conditions¹⁷, none of the available drugs may actually meet the patient's need. Understanding unmet need from the patient and caregiver perspective is critical. A recent report from an Externally-Led Patient-Focused Drug Development Meeting on Schizophrenia included findings from a patient and caregiver survey regarding reasons for stopping treatment. The reasons were many and varied, including that the medication did not treat the individual's symptoms, that the treatment led to weight gain, or that it caused movement effects such as tremor, stiffness, or agitation.¹⁸ Treatments that may ultimately address one or more of these barriers to patient adherence, and ultimately barriers to improved patient outcomes, compared to current medications should be assessed as meeting an unmet need.

As evidenced by the numerous references above, the very nature of mental health medications, and their well-defined lack of interchangeability and substitution on a patient-by-patient basis, means that nearly every mental health medication selected for negotiation will likely fill an unmet medical need for a significant cohort of the Medicare population. We call on CMS to clarify and broaden the definition of unmet need in consultation with patients, caregivers, and other affected stakeholders.

CMS Should Ensure that Mental Health Drugs Remain Broadly Accessible on Part D Formularies

The Guidance is also lacking clarity on whether and how Part D Plans must maintain access to both selected drugs and non-selected drugs following implementation of a negotiated price. Section 110 of the draft Guidance simply states: "In accordance with section 1860D-4(b)(3)(I) of the Act, Medicare Part D plans shall include each covered Part D drug that is a selected drug on Part D formularies during Contract Year (CY) 2026 and all subsequent years for which the MFP of the selected drug is in effect during the price applicability period." The draft Guidance does not state *how* Part D Plans are to "include" selected drugs, and is silent on the impacts on non-selected drugs in the same class. We are concerned that changing health plan incentives for drugs in a class where one or more drugs are negotiated could lead to negative formulary access consequences

¹⁷ <https://www.commonwealthfund.org/publications/explainer/2023/mar/medicare-mental-health-coverage-included-changed-gaps-remain>

¹⁸ <https://sczaction.org/wp-content/uploads/2023/02/Reimagine-Schizophrenia-VOP-report-FINAL.pdf>

(in the form of higher cost sharing, additional utilization management controls, and/or tiering). As CMS implements the negotiation program, the agency should ensure guardrails that prevent the erosion of important patient protections and policies that prevent discrimination in formulary design for certain patients, including those living with mental illness.

Such erosion would be devastating to those Medicare beneficiaries with SMI needing access to medications in these classes. We urge CMS to add guardrails into Section 110 to clarify that current beneficiary access, and the quality of that access, should not worsen as a consequence of MFP pricing in a particular class. CMS must take steps to ensure that beneficiaries retain access to the most clinically appropriate medication as determined by the provider and the patient. Adverse side effects that may result from taking the wrong medication frequently cause patients to discontinue their medication; this in turn leads to costly hospitalizations, relapses, and other harms to beneficiaries and to society.¹⁹

In 2018, the Pew Charitable Trusts found that, while restricting beneficiary access to select branded mental health drugs might generate some insurer savings from drug spend, “given the current high rates of generic use within the” therapeutic class, “there may be limited potential for savings from changes to this policy.”²⁰ The Pew findings echoed CMS’s own conclusions from 2014 when it estimated that repealing protections for two classes of drugs -- depression and immunosuppressants -- would save less than 0.4 percent of projected Medicare Part D spending in 2019. (Following opposition from many parties, Medicare withdrew this proposed change.)

State Medicaid programs have previously made attempts to limit patient access for mental health medications and have had to deal with the negative effects. For example, when Maine attempted to limit the antipsychotics included on its Medicaid formulary, tolerability issues contributed to unfavorable clinical outcomes and undermined the achievement of any savings. Noting a sharp rise in treatment discontinuities following the introduction of prior authorization (“PA”) for atypical antipsychotics (often called “AAs”), researchers stated that “[r]esponses to specific AAs and risks of adverse events

¹⁹ See, e.g., Kathleen Lang, et al., Medication Adherence and Hospitalization Among Patients with Schizophrenia Treated with Antipsychotics, *Psychiatric Serv.* 61.12 (2010): 1239-1247; Estimate of the Net Cost of a Prior Authorization Requirement for Certain Mental Health Medications, Driscoll & Fleeter (Aug. 2008), available at <http://www.namiohio.org/images/publications/Publications/EstimatedCostofPriorAuthorizationAugust20Final1.pdf>; see also Geils, *supra*, Incentivizing Drug Development in Serious Mental Illness.

²⁰ The Pew Charitable Trusts, “Policy Proposal: Revising Medicare’s Protected Classes Policy” (March 2018).

... vary. Thus, if certain patients are sensitive to adverse events associated with preferred agents, the PA policy could increase the incidence of unfavorable outcomes and contribute to medication discontinuation.”²¹ Maine suspended the restrictive access program nine months later because of “numerous case reports of adverse effects associated with the policy.”²²

A retrospective analysis of medical and pharmacy claims across 24 state Medicaid programs reported that patients with formulary restrictions had increased risks of hospitalization, lower adherence, and higher medical and prison costs.²³ A literature review of 15 studies of assessing the impact of formulary restrictions also concluded that drug cost containment policies may result in cost shifting rather than cost savings.²⁴ This volume of evidence further reinforces the need for CMS to maintain current access protections and prevent any potential narrowing of patient treatment options.

CONCLUSION

Drug development in SMI is associated with higher costs and higher risks than drug development for other chronic conditions. Regimes similar to the select drug Guidance, such as ex-US Health Technology Assessments, have significant delayed access to treatments and caused a reduction in available mental health medications.²⁵ In order to avoid potential serious adverse consequences for patients, CMS must take these concerns into consideration in evaluating its negotiation for any selected drugs for SMI by revising the draft guidance in close and continued consultation with all affected stakeholders. The availability of SMI drugs, and particularly newer next generation medications, to patients in need is already too low. The challenges to developing drugs in this therapeutic area are already high and will only be exacerbated with implementation of the negotiation program. Thus, we urge CMS to consider the comments above and to amend the Guidance to recognize the unique nature of these treatments.

²¹ Stephen B. Soumerai, et al., Use of atypical antipsychotic drugs for schizophrenia in Maine Medicaid following a policy change, *Health Affairs* 27.3 (2008): w185-w195 (internal citations omitted).

²² *Id.*

²³ Seabury, et al. Formulary restrictions on atypical antipsychotics; Impact on costs for patients with schizophrenia and bipolar disorder in Medicaid. *AJMC* 2014;20(2):e52-e60.

²⁴ Rajagopalan, et al. Review of outcomes associated with restricted access to atypical antipsychotics. *AJMC* 2016;22(6):e208-l 4.

²⁵ Tran, HTA decisions and access to mental health treatments in Canada’s public drug plans, available at <https://www.canadianhealthpolicy.com/product/hta-decisions-and-access-to-mental-health-treatments-in-canada-s-public-drug-plans-2/>



Thank you for considering Sunovion's comments and we look forward to continued opportunities for engagement with CMS on these critical issues. If you have questions, please contact me at eric.rasmussen@sunovion.com or (801) 870-7449.

Sincerely,

A handwritten signature in black ink that reads "Eric Rasmussen". The signature is fluid and cursive, with a long horizontal line extending from the end of the name.

Eric Rasmussen
Vice President, Government Relations & Public Affairs

April 11, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attn: PO Box 8016

Re: Medicare Drug Price Negotiation Program Guidance

Dear Centers for Medicare & Medicaid Services,

I write to you on behalf of my organization, Survivors for Solutions, to encourage you not to move forward with the agency's initial guidance for the Inflation Reduction Act's (IRA) Medicare Drug Price Negotiation Program. This guidance puts the health of millions of Americans in jeopardy, demeans our democracy by opening only the narrowest windows for these patients to offer their lived experiences, and belittles the voice of the patient – the most important stakeholder to this process – who will be most harmed by the IRA.

A 30-year survivor of multiple sclerosis, I founded Survivors for Solutions out of concerns for how little deliberation was given to such an impactful and extreme shift in policy such as the IRA. Made more grievous by the fast-tracked, party-line passage under the cloak of Covid lockdowns with little to no input from patients such as myself. Lawmakers enshrined price control schemes in a risky show attempt to address the high cost of a few drugs, choosing to ignore the real causes of high out of pocket costs that heavy price patients like me would have to ultimately and continue to pay. These mandates will significantly stunt the discovery of treatments and cures and slam the heavy hand of government interference onto the delicate ecosystem of the pharmaceutical research and development process. Some deep-pocketed special interests may not like the idea of paying for breakthrough treatments, but this is a critical aspect of what makes this country a leading force in delivering cutting-edge medicine to the world. Patients with health concerns ranging from cancers, chronic illnesses, and rare conditions need America's innovative ecosystem to thrive so that they may receive treatments that otherwise would not have been discovered. There are countless individuals that will be negatively impacted by fewer discoveries and less research, and it is up to our leaders to protect that hope.

The most affordable drug is the one that is never discovered. Our top biopharmaceutical research scientists put in time and effort to end suffering, dedicating years to the “trial and error” that comes with discovering new medicines to keep the pipeline of treatments flowing. Many patients, such as myself, must undergo multiple different treatments before we can find the one that works. The downstream effect of this price control gamble is that it will act as a disincentive to the company researchers that are critical for making future progress and creating multiple treatments for patients fighting to survive and desperate for the hope that additional options can deliver.

There are better ways to reduce drug costs for patients in this country, but the answer should never be to kill innovation and take away hope. Health care is about caring for people’s health, not CBO bean counters. The much-maligned research scientists have brought us the elimination of illnesses that were once deemed incurable; those are results that are simply too important to abandon.

Lastly, I cannot reiterate how arrogant, offensive, and un-democratic it is that this formal comment window is only open for thirty days – an atypical and extremely short timeframe. Patients, advocates, and those holding reservations about this guidance deserve more time to review the information and comment on this monumental alteration of our nation’s health system. Frankly, if you allowed a free and open public comment where people understood how much suffering, death, and despair this rule will bring about, there are not enough shelves in the Library of Congress to contain the outcry that would be unleashed.

Sincerely,

John Czwartacki

Founder and Chairman of Survivors for Solutions

www.survivorsforsolutions.org



April 14, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

Sutro Biopharma appreciates the opportunity to submit comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

Sutro Biopharma is a clinical stage company pioneering a unique way of discovering, developing, and manufacturing therapeutics. Our focus is aimed primarily on next-generation cancer therapeutics – antibody drug conjugates, bispecific antibodies, and cytokine derivatives. *While our company is working on biologics for the treatment of difficult to treat diseases, we can empathize with our peers at other companies who are working on small molecules that the IRA just made far less attractive to investors. It would have been our hope that our own drug, should it ever reach the market, could be used in combination or sequenced with those other medicines to meaningfully benefit and maybe even cure these diseases. We note that there are programs in development that may have to choose between an oral or biologic formulation, and the IRA would incentivize biologics over oral medicines.*

While we recognize that CMS is not formally accepting comments, we felt it was important to provide feedback into this new process.

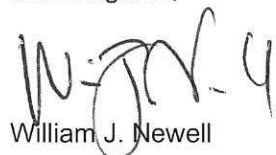
- I. Section 30.1: Medicare negotiation for NDA-path drugs at nine-years post launch severely restricts the financial opportunity to recoup the significant costs invested in research, development, and manufacturing to bring an approved product to market. And unfortunately, many products fail in clinical trials and associated costs are lost. Also, erosion of the investment case for small molecules may influence companies to develop biologics over small molecules, which may not be favorable for patient convenience and experience. We recommend extending exclusivity to 13 instead of 9 years.
- II. Section 30.1.1 Unfairly penalizes drugs that can benefit multiple orphan or rare diseases and would limit patient benefit and dis-incentivize development in novel ways. Alternatively, CMS should look to consider only active orphan drug designations for the purposes of determining

eligibility for the orphan drug exclusion and not including withdrawn orphan drug designations.

- III. Section 50. Cost-effectiveness evaluations like ICER tend to underestimate value of new medicines. Many countries that rely on these evaluations also experience significant delays in access to innovative medicines. Alternatively, CMS should consider broader evaluations of cost effectiveness, highlighting key product attributes like efficacy, safety and ease of use in determining relevant "therapeutic alternatives."
- IV. Section 90.4 Drives prices down inadvertently threatens the competition and viability of biosimilars and generic medications, which would negatively impact the overall costs across the market.
- V. Section 40.2.2 Lack of transparency on CMS criteria on MFP leads to great uncertainty and ambiguity on what is needed to justify price negotiations and access to innovative medicines. This will negatively impact investor confidence and increase risks to products even after they are approved.

We appreciate your consideration of our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to seniors from fewer innovative medicines is minimized. Please contact me by telephone or e-mail below if you have any questions regarding our comments.

Best Regards,



William J. Newell
CEO
Sutro Biopharma
Cell (650) 863-6480
bnewell@sutrobio.com



Submitted electronically Friday April 14, 2023 to IRAREbateandNegotiation@cms.hhs.gov

To: Meena Seshamani
CMS Deputy Administrator and Director of the
Center for Medicare
7500 Security Boulevard
Baltimore, MD 21244

To: Chiquita Brooks-LaSure
CMS Administrator
7500 Security Boulevard
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program Guidance

T1International is grateful for the opportunity to provide comments to CMS regarding Medicare Drug Price Negotiation Program Guidance.

T1International is a global diabetes advocacy organization led by and for people with diabetes. We believe in a world where everyone with diabetes, no matter where they live, has everything they need to survive and achieve their dreams. We do not accept funding from the pharmaceutical companies and we provide advocacy training and support to advocates across the U.S. and around the world. In 2014, T1International launched the #insulin4all campaign which has grown into a global movement. In the U.S., T1International supports advocates via 41 #insulin4all Chapters, our Federal Working Group, and through our Global Advocacy Network.

At T1International, our global advocacy goal is that the average combined monthly out-of-pocket cost of insulin and blood glucose testing supplies for people with diabetes will represent no more than 5% of median income in any given country by 2025. Our campaign priorities include a federal price cap on insulin, patent reform, tax reform, emergency access to insulin laws (Alec's laws), expanding pharmacist scope of practice (Kevin's Laws), expanding public production and public procurement of insulin and other drugs, and reforming insurance formularies to eliminate non-medical mid-year plan switching.

As patients working on insulin access and affordability, we are frustrated with the lack of explicit insulin price negotiations included in this bill. Recent insulin manufacturers announcements of lowering the list prices of several insulin products does not go far enough; to meet patients' full needs, these price decreases must apply to all insulin products, must be codified, and must be negotiated in a fair and transparent manner. We appreciate CMS developing guidance that minimizes opportunities for manufacturers to undermine the intention of the Inflation Reduction Act by closing loopholes regarding many predatory business strategies, anti-competitive tactics, abusive pricing and general market manipulation. We hope the identification of selected drugs for initial price applicability sets a strong standard for future drug negotiations, including for insulins.

Product hopping prevention measures are critical for patients using insulin and other drugs. We support defining single source drugs by aggregating across all dosage forms and strengths. Doing so will prevent some potential gaming that we have seen run rampant in the insulin market. For example, vials and pens have different prices due to different patent evergreening practices, and patients have been changed to newer, more expensive insulin prescriptions without their prior notification. We urge CMS to





ensure that competing products are defined so as to require a meaningful market penetration and easy accessibility by patients, to prevent potential gaming by product hopping.

Scrutiny around biosimilar delay requests is an important first step. Insulin manufacturers have wielded the existence of captive generics and modest biosimilar competition by competing manufacturers to avoid some scrutiny. This cartel-like behavior has resulted in a lack of meaningful competition and lower prices, since captive generics have historically not been available in pharmacies and biosimilars of many important biologic drugs have made only modest headway against their entrenched competitors. Biosimilars must be available and accessible to patients at pharmacy counters to actually bring down drug prices.

Drug prices are already too high. We cannot look at net price or average sale price as a key factor to set maximum fair price as they are already inflated. In the insulin market, the lack of industry competition means that net prices are too high. Consequently, using the prices of therapeutic alternatives as a starting point will lead to inappropriately high prices. Therefore, we should instead look at the cost of manufacturing with adjustments for clinical benefits, which will continue to incentivize innovation.

Patients need access to maximum fair prices in a clear and cohesive way. To effectively price affordable drugs and to amplify the impact of the IRA, industry pricing data needs to be collected with detail and openly published so that it is accessible. Collection and publication of disaggregated figures on R&D costs, for example, can allow explanation and public discussion of the maximum fair price. This level of transparency will set an important precedent for patients. For example, Colorado's prescription drug price transparency bill (HB19-1131), which has manufacturers provide WAC prices, is interpreted differently by every manufacturer, making accessing and interpreting the information challenging for patients. If CMS regulated cost transparency, reporting would be consolidated, streamlined, and consistent, and patients and advocates would be better able to navigate the prices.

Real, meaningful, and diverse penalties are needed for effective enforcement. Civil monetary penalties of \$1mil/day for violating terms of the negotiated agreement and \$100mil for submission of false information will increase the likelihood of the negotiation process yielding the intended outcome: fair prices at the pharmacy counter.

The process needs to center patient involvement and experience. Expanding opportunities for independent patient advocates, patient advocacy groups, and consumer groups will improve processes and practices. This is especially true for those of underrepresented demographics and communities, including those in different age groups, races, and the LGBTQIA+ community. We want to ensure that [ethical patient engagement principles](#) are followed in the process.

From:
Shaina Kasper
Policy Manager, USA
T1International



April 14, 2023

The Honorable Xavier Becerra
Secretary
Department of Health and Human Services
200 Independence Avenue, SW
Washington, D.C. 20201

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Dear Secretary Becerra and Administrator Brooks-LaSure:

The Taxpayers Protection Alliance (TPA) writes today on behalf of taxpayers and consumers to voice our concern regarding the Centers for Medicare & Medicaid Services' (CMS) initial guidance on the drug pricing provisions in the Inflation Reduction Act (IRA). We urge you to reconsider advancing these provisions that would pose irreparable harm to the future of American healthcare and patients.

TPA has been critical of how the highly partisan IRA's price-setting policies threaten the development of potential lifesaving cures to the detriment of all American consumers. CMS' initial guidance doubles down on this damage by creating a process with minimal transparency that prioritizes the government's interests over those of patients. This represents a further encroachment of the federal government into the successful U.S. pharmaceutical system that provides American patients with the greatest access to critical cures of any country in the world.

CMS' initial guidance endangers the types of intellectual property (IP) protections that are the very lifeblood of pharmaceutical innovation. IP protections are critical to incentivizing pharmaceutical companies to invest the time and resources needed to explore potential cures because they give companies assurance that they will be rewarded for their risks if a drug is proven effective.

Targeting drugs for the length of their exclusivities and patents takes away incentives to innovate, meaning fewer companies will invest in exploring potential lifesaving cures for American patients. The Biden administration has championed its commitment to finding a cure to cancer. That won't be possible if there's no incentive to innovate, particularly when it comes to post-approval research.

We urge you to do what's in the best interest of American consumers and reconsider this rule.

Sincerely,



David Williams
President

April 14, 2023

The Honorable Meena Seshamani, M.D., PhD.
Deputy Administrator and Director of the Center for Medicare
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, Solicitation of Comments

Dear Deputy Administrator and Director Seshamani:

The ALS Association is pleased to provide comments on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026.

As the world's leading ALS organization, our goal is to make ALS livable for everyone, everywhere, until we cure it. Established in 1985, The ALS Association is the only national nonprofit organization fighting ALS on every front. By leading the way in global research, coordinating multidisciplinary care through certified clinical care centers, and fostering policy solutions, we strive to make ALS a livable disease while aggressively searching for new treatments and a cure. We are committed to ensuring all people with ALS have access to medical products and services that enhance their health and wellbeing and improve their quality of life.

In the drug pricing debate, our primary goal is to ensure equitable access to treatments. We are constantly taking into consideration ways to support efforts to reduce drug prices with the need to safeguard the pace of innovation and protect access to new therapies. This is particularly important for treatments that impact people with rare diseases, as barriers to developing new treatments are already high. Additionally, we are particularly concerned with any cost-cutting efforts that may disincentivize drug development and devalue treatments options for people living with Amyotrophic Lateral Sclerosis (ALS), those with disabilities, or the terminally ill.

The ALS Association remains concerned about timely access to innovative treatments. Solutions must be balanced to ensure individuals do not have to face even more barriers to treatments. Congress has recognized the unique nature of rare diseases and we are hopeful CMS will also work persistently to protect access to drugs for rare disease populations as Inflation Reduction Act (IRA) implementation takes shape.

Thus, we support the Centers for Medicare and Medicaid Services (CMS)'s program to reduce drug prices via the Medicare Drug Price Negotiation Program as required by IRA but offer comments herein on ways to ensure cost benefits and equitable access to therapies are secured for people living with ALS, the acutely ill, and people with disabilities.



OUR VISION: Create a world without ALS.

OUR MISSION: To discover treatments and a cure for ALS, and to serve, advocate for, and empower people affected by ALS to live their lives to the fullest.

HOME OFFICE • 1300 Wilson Boulevard, Suite 600, Arlington, VA 22209 • PHONE 202.407.8580 FAX 202.464.8869 • [als.org](https://www.als.org)

Ensure people living with ALS benefit from lower drug prices:

We are supportive of the provisions that require negotiated products within the Medicare Part D program to be included on Part D plan formularies. It is important that CMS ensures rare disease patients benefit from all drug price negotiation efforts to reduce out of pocket costs, establish premium caps, and maintain timely access to drugs. Often, therapies that treat rare diseases are placed on the specialty tier of plan formularies, resulting in significant out-of-pocket costs and access delays for Medicare beneficiaries. Once a drug is negotiated and appropriately priced it should be placed on a lower formulary tier to reduce patient out-of-pocket costs and pass on savings to patients.

Discontinue the use of unreliable and discriminatory methodologies in drug price negotiations:

An unfortunate source of treatment delays or denials for the ALS community are the inequitable use of comparative clinical effectiveness research and utilization management tools used by payers to support economic, scientific, legal, and or public policy rationales. We appreciate the intent of Congress to protect vulnerable populations through IRA by including key provisions, such as, “the Secretary shall not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, non-disabled, or not terminally ill.”^{iv} While it is not an explicit component of the IRA, we also want to express our strong objections to the quality-adjusted life year (QALY) methodology used by some organizations to assess the “cost-effectiveness” of therapies. We believe this approach devalues the life of a person living with ALS and is therefore fundamentally flawed and not equitable.

As previously stated in our February 13, 2023, public comments on *Contract Year 2024 Policy and Technical Changes* [CMS-4201-P], we strongly support CMS’s proposals to clarify and revise the regulations governing when and how Medicare Advantage plans develop and use coverage criteria and utilization management policies to improve health equity for people with disabilities. The use of prior authorization for people with rare diseases too often causes unnecessary delays and denials even though requested therapies meet Medicare coverage guidelines. We agree with CMS proposed policies to improve prior authorization policies and we implore the agency to universally apply protections to Medicare Advantage enrollees and ensure equivalency with Traditional Medicare coverage policies.

We urge CMS to require Medicare Part D plans to reduce or eliminate the use of utilization management tools which unnecessarily delay essential care, including prior authorization, to ensure people with rare diseases – especially people living with ALS – have timely and broad access to negotiated drug therapies and associated cost savings.

Avoid disrupting research and innovation of therapies for rare diseases:

As mentioned, barriers to drug development for rare conditions are extremely high. Small disease populations have difficulty recruiting patients for clinical trials and managing disincentives for investment. We appreciate CMS’ recognition of this phenomenon by excluding orphan drugs from drug price negotiations. However, additional clarity could be provided about how that exclusion functions and these protections are applied. Additionally, we recommend that CMS maintain the exclusion for orphan drugs that have more than one indication. If not, drugmakers will be disincentivized from pursuing additional indications that could be beneficial.

Avoid the use of tools that do not adequately capture value:

The ALS Association joins the National Council on Disability and other patient advocacy organizations representing patients and people with rare diseases and disabilities on the position that clinical

comparative effectiveness research tools, such as incremental quality adjusted life years (QALYs) and equal value of life years gained (evLYG) metrics, do not fully capture patient preferences and societal value of therapies for people living with ALS and can be inherently discriminatory. Fortunately, the IRA explicitly prohibits the use of comparative clinical effectiveness research in such a way that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, non-disabled, or not terminally ill and specifically clarifies that CMS cannot rely on discriminatory metrics like QALY.

We are concerned that section 50.2 of this draft guidance indicates that CMS will consider studies that use QALYs. CMS should reiterate in its guidance that it will not rely on QALYs or similarly discriminatory metrics in the evaluation of drug therapies. Instead, CMS should define comparative clinical effectiveness research in a manner consistent with the existing definition in the Affordable Care Act (ACA), which clearly defines the research as comparing clinical benefit and not cost or cost-effectiveness. In determining what comparative effectiveness research to rely on, CMS should look to a robust body of ongoing research that includes patient-centered input, measures therapeutic benefit to patients, and engages patients and people with disabilities to understand their perspectives on quality of life and preferred outcomes and experiences.

Continue robust engagement of rare disease patients and people with disabilities:

We appreciate the opportunity to comment on this draft guidance and to continue to engage with CMS on these and other efforts to reduce drug prices and out of pocket costs for people living with ALS. We strongly encourage CMS to maintain continual engagement with the patients and with organizations that represent their interests. Ensuring these voices are a part of the process will ensure policies are patient-centered and value-based.

Recommendations:

In summary, we urge CMS to i) simplify and streamline the data submission process for patients and caregivers; ii) clarify what information the agency is seeking from patients and in what format to allow for data standardization and aggregation, iii) organize patient listening sessions specific to selected drugs to collect representative data while CMS is preparing the initial offer for a negotiated price; and iv) include consistent and granular summaries of the data and assumptions on which each negotiation was based on, including patient experience data.

We look forward to continual opportunities to engage with CMS on these and other topics and provide valuable insights on issues of importance to people living with ALS and their family members. Should you have any questions, please contact Rich Brennan, Vice President of Federal Affairs at rich.brennan@als.org.

Sincerely,



Melanie Lendnal, Esq.
Senior Vice President, Policy and Advocacy

ⁱ <https://www.congress.gov/bill/117th-congress/house-bill/5376/text>

4/12/2023

Dr. Meena Seshamani, M.D. Ph.D.,
CMS Deputy Administrator and Director of the Center for Medicare
5600 Fishers Lane
Rockville, MD 20857

RE: Medicare Drug Price Negotiation Program Guidance

Attention: IRRebateandNegotiation@cms.hhs.gov

Deputy Administrator Seshamani:

As Senior Vice President of Industry Relations for Sentry Data Systems, now The Craneware Group, I am pleased to have the opportunity to comment on the above referenced memorandums specific to the 340B Discount Drug Program administered by Health Resources and Services Administration (HRSA). We have previously commented on other matters and our emphasis is on Providing Access to the Maximum Fair Price (MFP) (40.4) and nonduplication with 340B Ceiling Price (40.4.1).

Sentry Data Systems, a pioneer in automated pharmacy procurement, utilization management and 340B compliance, is leading the industry in helping healthcare organizations address their three biggest challenges: reducing costs, managing compliance and improving outcomes. More than 10,000 hospitals, clinics, integrated delivery networks (IDNs) and pharmacies across the country rely on our integrated platform for their procurement, drug utilization and compliance solutions.

In July 2021, Craneware announced the acquisition of Sentry Data Systems and Agilum Healthcare, optimizing an already-robust catalog of solutions. Now, after more than 20 years as the leading provider of revenue integrity solutions improving financial performance in U.S. hospital and health systems, together, we are The Craneware Group¹ and we deliver software applications across the value cycle.

The Craneware Group (AIM:CRW.L), the market leader in automated value cycle solutions, including 340B management, collaborates with U.S. healthcare providers to plan, execute, and monitor operational and financial performance so they can continue to deliver quality care to their communities. Customers choose The Craneware Group's Trisus data and applications platform as their key to navigating the journey to financially sustainable value-based care. Trisus combines revenue integrity, cost management, 340B performance, and decision enablement into a single, SaaS-based platform. Trisus Chargemaster secured top ranking in the Chargemaster Management category of the "2023 Best in KLAS Awards: Software & Services" and is part of an extensive value cycle management suite. The Craneware Group – transforming the business of healthcare.

¹ The Craneware Group accessed 3/8/2023 <https://www.thecranewaregroup.com/company/our-story/>

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Maximum Fair Price Access

Maximum Fair Price

Restating previous comments provided to CMS in March 2023, 340B covered entities may not utilize 340B purchased drugs if the maximum fair price is less than the 340B purchase price. In these instances, covered entities will not be required to utilize the JG or TB modifier for Part B Claims, and similarly for Part D Claims; those claims will need to be subject to inflation reduction rebates.

Maximum Fair Price and Contract Pharmacies

340B covered entities may choose to contract with pharmacies on their behalf to dispense 340B to eligible patients, that may also be considered MFP-eligible individuals (patients) for the purposes of Medicare Part D. It is important that MFP pricing be available through bill to-ship to mechanisms. This entails that billing is sent to the 340B covered entity, and drug product is shipped to the contract pharmacy when eligible patients receive prescription benefits on behalf of the covered entity. Any differences between acquisition cost for the selected drug and the MFP would need to be reimbursed timely through the appropriate contract pharmacy wholesaler or manufacturer direct purchase accounts or third-party logistics (3PL) companies within 14 days without any transaction fee. It is important to note that manufacturers have implemented practices related to contract pharmacy that do not align with the law as noted by recent HRSA communications to certain manufacturers². Additionally, 3PL companies have placed barriers to receiving 340B price and should also make available MFP pricing on selected drugs. Making the MFP available to covered entities and their contract pharmacies is essential to carrying out the Inflation Reduction Act.

Nonduplication with 340B Ceiling Price

While manufacturers have been required by the 340B statute to provide 340B Ceiling Price, it should be noted that not all manufacturers with a focus on high-cost specialty drugs make 340B pricing consistently available to covered entities. We encourage CMS to make available the MFP to 340B covered entities to allow them the opportunity to purchase at the best price available to them.

HRSA Office of Pharmacy Affairs Information System (OPAIS)

While the spirit of the IRA is to avoid nonduplication of 340B Ceiling Price, it is imperative to recognize that MFA will need to be added to the HRSA Office of Pharmacy Affairs Information System (OPAIS) an indicator for both 340B and MFP pricing. As a software company responsible for processing 340B eligible claims based on 340B price, and now MFP pricing, it would greatly assist us to have limited access to the price file on behalf of the covered entity to validate price file data received from wholesalers to data in OPAIS. The limitations of the OPAIS system today, do not allow for third-party access to support covered entities determine accurate pricing, outside of the wholesaler or the covered entity making inquiries without the assistance of software.

Price File Updates

MPF should be provided by the wholesaler on the 340B price file to covered entities with an indicator that it is an MFP. Wholesalers can include indicators on the type of pricing provided (340B Prime Vendor Program sub-ceiling price, 340B, WAC). If MFP is available at 340B price, both prices should be supplied on the price file. The wholesaler acquisition price (WAC) file should always include the MFP. Unique to the 340B program is the group purchasing organization (GPO) prohibition for certain types of hospitals, often requiring them to purchase on WAC versus 340B. Additionally, GPOs often repackage drugs and sale at a GPO price, which certain 340B covered

² Health Resources and Services Administration Office of Pharmacy Affairs HRSA Correspondence to Stakeholders accessed 4/12/2023 <https://www.hrsa.gov/opa/program-integrity>

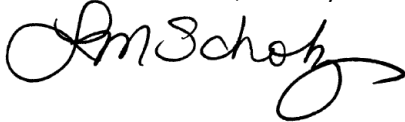
entities with GPO prohibition criteria, are not allowed to utilize. It will be important that GPO repackaged drugs, also have MFP available when appropriate. These price file changes assist covered entities determine whether a 340B price or MFP price is the lower price using technology versus manual look-ups of the OPAIS. Software solutions then have “best price” functionality that can assist determine which price should be used and subsequently place appropriate modifiers based on price and assist with the true-up process for drugs indicated as an MFP at the time of dispensation, including retrospective changes. The current process supported by HRSA is available for both covered entities and manufacturers to dispute price discrepancies. We would encourage a standard format for submitting to manufacturers for price variations between MPF and 340B with HRSA and CMS.

Thank you for the opportunity to provide comments on behalf of The Craneware Group and for your time to consider our recommendations. We welcome providing our insights into the IRA process to support covered entities manage the complexity of 340B in the current environment with a look to the future to make it accessible and fair for the safety net- the ultimate beneficiary of the 340B program. The 340B program allows the covered entities to serve their communities offering more comprehensive care—therefore having a comprehensive and efficient revenue integrity process allows them to continue to focus on what they do best- care for patients.

We would be happy to provide more real-world operational information or answer any questions.

Regards,

Lisa Scholz, PharmD, MBA, FACHE
Senior Vice President, Industry Relations



April 14, 2023

Dear Administrator Brooks-LaSure,

The Foundation for Research on Equal Opportunity (FREOPP) writes in response to proposed guidance published on March 15, 2023, implementing the Medicare drug price negotiation program as enacted in the Inflation Reduction Act (IRA). FREOPP is a non-profit, non-partisan think tank that seeks to expand economic opportunity to those who least have it, using the tools of individual liberty, economic freedom, technological innovation, and pluralism. All of our research and policy recommendations considers the impact on those below median income and wealth.

The IRA's drug price negotiation program represents a welcome change to the status quo for Medicare drug spending. Our research recognizes that one of the biggest drivers of rising drug spending comes from pharmaceutical companies increasing prices on branded drugs that have been on the market for several years. The IRA appropriately selects drugs for price negotiation that are nearing the end of their patent and FDA exclusivity timelines while driving significant savings for Medicare and the beneficiaries it serves.

We also applaud CMS' regulatory change to the meaning of "gross covered prescription costs," as outlined in CMS' proposed rule dated December 27, 2022. The change ensures that drugs will be selected for negotiation based on total gross expenditures in Medicare, rather than net expenditures. In turn, the change potentially disincentivizes drug companies from using large rebates to get better formulary placement, leading to lower out-of-pocket costs for seniors.

However, we recognize certain aspects of implementation could be clarified or improved. There are two aspects of CMS guidance on Medicare Drug Price Negotiation Program implementation that demand special attention.

1. *Impacts to generic development.* Though the IRA will reduce Medicare drug spending by \$102 billion over the next 10 years, the most effective mechanism for drug cost savings is competition. The Drug Price Competition and Patent Term Restoration Act, aka Hatch-Waxman Act, is proof that competition from generics can drive immense savings for Americans.

Therefore, CMS must walk a careful line between maximizing Medicare drug savings through the IRA and fostering a healthy generics market that allows generics and biosimilars to quickly grow market share.

Unfortunately, CMS guidance falls short in this area in a key way.

The IRA provides two conditions by which a selected drug is removed from the drug price negotiation program: the generic or biosimilar that references the selected drug must first be approved by the FDA, and then it must be "marketed" pursuant to such approval.

According to guidance, CMS will review the previous 12 months of Medicare prescription drug data to determine if a company has engaged in "bona fide marketing" of the generic or biosimilar only after CMS has determined such drug has been approved by the FDA. This implies

that, should a generic be recently approved, CMS would wait to receive 12 months of sales data before determining if the drug has reached a satisfactory level of marketing to remove the branded reference product from negotiation. In addition, CMS is silent on the sales thresholds during the 12 months that it believes reaches the level of bona fide marketing.

CMS risks unnecessarily delaying the removal of an MFP from a selected drug if it requires 12 months of sales data to determine if the drug is marketed or if CMS sets a high sales threshold to achieve bona fide marketing. We believe that the longer an MFP remains in effect, the more difficult it will be for generic or biosimilar drugs to gain market share.

Therefore, we recommend CMS clarify its timeline for considering whether a generic or biosimilar exists for a selected drug, and to make such determinations as soon as practical to minimize disruption of generic drug launches.

2. *Information disclosed for explanation of MFP.* Following negotiations and determination of the MFP, CMS will publish the MFP for each drug along with an explanation of how it arrived at the MFP according to factors outlined in Sec. 1194(e) of the IRA. According to the March 15 guidance, “CMS intends to make high-level comments on the data submitted to CMS, without sharing any proprietary information.”

The IRA empowers the Secretary to determine what information provided by drug companies is proprietary for the purposes of carrying out price negotiation. Pursuant to such authority, CMS intends to define proprietary information as “commercial or financial information of the Primary Manufacturer or a Secondary Manufacturer that cannot be found publicly.”

Thus, CMS intends to treat the following company-provided data as proprietary information:

- a. Research and development costs and recoupment,
- b. Unit costs of production and distribution,
- c. Pending patent applications,
- d. Market data, and
- e. Revenue and sales volume data.

By treating such information as proprietary, we believe CMS has missed an extraordinary opportunity to shed light on how pharmaceutical prices are set throughout the pharmaceutical market. We also believe there is a substantial public interest in releasing such information. We could answer vital questions, such as root causes of rising drug prices in the U.S., whether high prices are justified on the basis of high R&D costs, and how companies use the patent system to stymie competition.

Guidance indicates CMS seeks to protect proprietary information so that companies will be more likely to cooperate with CMS and engage in the negotiation process. In this regard, we believe CMS is proceeding with too much caution. In particular, market data and revenue and sales data may be considered proprietary by pharmaceutical companies, but this data is in fact available to many stakeholders through subscription services such as SSR Health and IQVIA.

While it is understandable that CMS prefers full cooperation from drug makers, we believe that the possibility of civil monetary penalties, as outlined in Section 1197 of the IRA, will motivate

drug companies to comply with program requirements, including the submission of data to inform CMS' negotiation efforts.

We recommend CMS clarify when it considers company data is available to the public and thus non-proprietary. We also recommend CMS use its regulatory authority to release as much data as is legally possible when publishing the MFP and explanations of the factors influencing the MFP.

We appreciate the opportunity to provide comment on these important matters as CMS implements the Medicare Drug Price Negotiation Program. We welcome further dialogue to ensure the program reduces drug spending in Medicare while enhancing drug price competition in the wider pharmaceutical market.



April 14, 2023

Meena Seshamani, MD, PhD
Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

**Re: Medicare Drug Price Negotiation Program: Initial Memorandum,
Implementation of Sections 1191-1198 of the Social Security Act for Initial Price
Applicability Year 2026, and Solicitation of Comments**

Dear Deputy Administrator Seshamani:

The Leukemia & Lymphoma Society (LLS) appreciates the opportunity to provide comment on this initial guidance implementing the Inflation Reduction Act (IRA)'s drug price negotiation program. LLS's mission is to cure leukemia, lymphoma, Hodgkin's disease, and myeloma, and to improve the quality of life of patients and their families. We advance that mission by advocating that blood cancer patients have sustainable access to quality, affordable, coordinated health care, regardless of the source of their coverage.

Input Regarding Clinical Benefit and Patient Engagement

Patient engagement is an important step to better understanding how patients view the burden of their disease, their desired treatment outcomes, and their views on benefits and risks associated with the range of treatments available to them. Driven by the work of the Food and Drug Administration (FDA) on patient-focused drug development (PFDD), many drugmakers have worked with FDA and patient organizations to develop quantitative and qualitative data that allows regulators and other stakeholders to better understand the needs of particular patient populations and the extent to which a drug meets those needs. We encourage CMS to consider the positive impact of appropriately incorporating PFDD data and similar data that may help CMS better understand the extent to which a given product represents a therapeutic advancement over other products and/or meets a patient need that is otherwise unmet by other products.

We ask CMS to provide more clarity on how the agency intends to leverage negotiation data, to ensure that the agency is evaluating these elements with the patients' experiences, preferred outcomes, and needs in mind. For instance, we ask that CMS transparently outline a consistent methodology for how data related to therapeutic alternatives will result in changes to an initial or final offer. As part of this methodology, we ask that CMS ensure data explicitly related to patient value is prioritized. CMS should appropriately prioritize patient experience

data among the many factors CMS identifies in the guidance as sources that will inform an initial/final offer. Following negotiation for a particular product, we encourage CMS to articulate how patient experience data influenced initial and final offers.

In addition to the opportunity to submit data, LLS urges CMS to develop further initiatives to solicit feedback from the patient community. These processes could be comparable to the FDA's work in PFDD. CMS should develop a patient engagement infrastructure that creates an ongoing dialogue with patient communities whose patients may be prescribed drugs that have been selected for negotiation.

Maintaining and Improving Beneficiary Protections

We appreciate the IRA's provision requiring all Part D plans to cover each drug with negotiated prices for all years for which the price is in effect during the price-applicability period. This provision helps ensure that beneficiaries will benefit from the negotiation process and have access to the lowest-price drugs.

LLS encourages CMS to monitor Part D plans to ensure beneficiaries have access to all negotiated drugs and provide opportunities to comment on beneficiary protections in the future. Additionally, we urge CMS to require Part D plans to reduce or eliminate burdensome utilization management (UM) tools and prohibit plans from placing negotiated drugs on a formulary tier requiring cost-sharing calculated by co-insurance rather than a flat copay.

The initial guidance did not address UM tools (e.g., step therapy, prior authorization, etc.) or cost-sharing requirements employed by Part D plans with respect to negotiated drugs. UM techniques and cost-sharing requirements can create significant barriers and increase costs for patients by delaying the start or continuation of necessary treatment and negatively affecting patient health outcomes. Thus, it is critical that CMS create guardrails to ensure plans facilitate appropriate access to medicines by limiting these burdensome barriers, especially when the drug in question has an established maximum fair price. LLS believes this step would reduce the risk of plans delaying or denying access to products vital to a patient's care plan.

CMS must closely monitor plans as they adjust formularies due to these new incentives, as CMS will likely need to create new, more patient-friendly consumer protections to facilitate patient access to clinically-necessary off-formulary drugs.

Maintaining Incentives for Additional Indications

The IRA made significant changes to the incentives for drugmakers to invest in new indications for drugs they are bringing or have brought to market. The previous financial incentives for this investment were far from perfect, but it's clear they encouraged investments in supplemental indications. The IRA ushers in a new era with different incentives, and stakeholders are closely monitoring the effect of these new incentives.

As we monitor the effects of these new incentives, it is prudent to consider opportunities to reinforce the kind of investments that have led to new indications with proven value for patients. In that spirit, we encourage CMS to consider opportunities to promote a drugmaker's investment in research and development – opportunities aimed specifically at identifying supplemental indications, particularly indications for small populations, pediatric populations, and for populations with unmet needs. For example, CMS could use such investment as a factor in considering which products are selected for negotiation or in determining an initial or final offer during the negotiation process.

Utilization of Quality-Adjusted Life-Years (QALYs) in the Negotiation Process

LLS supports CMS's interpretation of the IRA as requiring the agency to separate out and exclude QALY metrics from the analysis of evidence in value-based decisions.

LLS believes that any evidence that values extending the life of some individuals less than extending the life of other individuals based on disability status, age, or membership in other special populations (e.g., children or those of marginalized status, including the patient community of color) is completely inappropriate. All patients deserve to be treated equally.

LLS agrees with CMS that negotiation would benefit from access to additional types of measures as a base for evaluation. While we cannot provide specific recommendations at this time, it is important that CMS does not rely on a single metric and instead looks widely at sources to take a holistic approach.

Orphan Drug Exemption

We appreciate that the IRA includes a limited exemption from drug price negotiation for orphan drugs that only treat one rare disease. However, we are concerned about CMS's current interpretation of this exemption. That interpretation would make products eligible for negotiation once they have been designated for two or more orphan diseases, even if a product is not yet FDA-approved to treat the second orphan disease. Our concern is that this might disincentivize drug companies from conducting even the basic research necessary to develop a drug for additional rare diseases, as designating a drug for a rare disease is done very early on in the drug development process, far in advance of when a company would be permitted even to market a drug for that specific condition. We urge CMS to clarify that obtaining additional designations for a small molecule or biologic will not make a drug negotiation-eligible until the drug has been approved by FDA to treat a second disease or condition.

Conclusion

LLS thanks CMS again for its leadership in this critical area and for this opportunity to provide comment on this important guidance. If you have any questions or would like to discuss our



LEUKEMIA &
LYMPHOMA
SOCIETY®

comments further, please contact Phil Waters, Director, Federal Public Policy, at at
phil.waters@lls.org.

Sincerely,

Bethany Lilly
Executive Director, Public Policy

April 12, 2023

Center for Medicare and Medicaid Services
Attn: IRAREbateandNegotiation@cms.hhs.gov

RE: Medicare Drug Price Negotiation Program Guidance

To Whom it May Concern:

I am writing to you today to express my support for the use of cost-effectiveness analysis (CEA) as a critical input into data collection and analysis for drug price negotiation to support the Medicare program. I recognize that CMS is excluding consideration of the quality-adjusted life year (QALY) as a measure of health gain in such analyses, due to concerns that the measure may somehow value extending the life of an elderly, disabled, or terminally ill individual at a lower level than that of a younger or healthier individual. I disagree with this approach because, in practice, QALYs are used to compare the effects of treatments, not to value the life of an individual in the absolute.

Nevertheless, there are alternatives to the QALY that take different approaches to measuring and valuing life extension. For example, the equal-value life year ([evLY](#)) and health years in total ([HYT](#)) are two approaches to valuing life extension from treatment on an equal footing across diseases and patient populations. The *disability*-adjusted life year ([DALY](#)), used widely in the developing world, actively measures the level of disability and premature loss of life caused by disease, with the intent of rewarding innovations that reduce these effects. Finally, a new approach, known as Generalized Risk-Adjusted Cost-Effectiveness ([GRACE](#)) Analysis, allows for improvements in quality of life to be weighted more heavily for disabling and severe conditions. All of these measures, applied with care and consideration, meet the intent of the statute that excludes QALYs, because they all treat life extension on an equal footing.

The alternative measures specified above do not exist in isolation; rather, they are used like the QALY is as a key component of CEA. If CMS also restricts or eliminates the use of these alternatives, there is little left upon which to base CEA. Using a simpler measure like "[life years](#)", for example, would only reward treatments that extend life, not those that act primarily to improve quality of life. This would severely underestimate benefits that might be gained from new treatments for multiple sclerosis, psoriasis, arthritis, and many other conditions that greatly diminish function and quality of life.

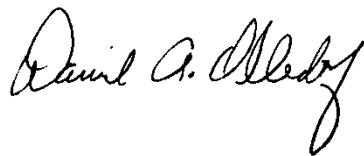
In sum, these concerns do not come from a standpoint of technical jargon and academic preferences; rather, it is that I strongly believe that elimination of CEA and other economic analysis to inform health decisions will harm the very populations the QALY-eliminating language seeks to protect. Without such analyses, insurers (including plan sponsors participating in Part D) can resort to placing severe restrictions on access to medications and creating multiple hoops for patients to



jump through as a way of saving money, without paying any attention to the potentially significant value that new (albeit expensive) treatments might bring. I have witnessed, and strongly support, great levels of innovation over the last decade, innovation that has changed the lives of patients and families. Analyses such as CEA can help ensure the health system is investing in those types of innovations and paying fairly for them; this will serve to send the right signals to industry about the type of innovation we as a society want.

Please do not hesitate to contact me should have any questions or require clarification.

Sincerely,

A handwritten signature in black ink, reading "Daniel A. Ollendorf". The signature is written in a cursive, flowing style.

Daniel A. Ollendorf, PhD
Director of Value Measurement and Global Health Initiatives
Center for the Evaluation of Value and Risk in Health (CEVR)
Tufts Medicine





April 14, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building, Room 445-G
200 Independence Avenue, SW
Washington DC 20201
IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure,

While we don't believe that legislators who approved the Inflation Reduction Act (IRA) intended to stop or dissuade the development of life-saving drugs, that is one of the unfortunate consequences of the IRA.

We are Tyra Biosciences, a San Diego based company, and one of many emerging biotechnology companies that face shareholder pressure to reconsider the clinical development pathway for our drug candidates in certain indications as a direct result of the IRA. In our case, the IRA provides a disincentive to continue the development of an oral cancer treatment that we believe has the promise to be more effective than current therapies, including providing for an easier and more convenient oral administration over daily injections or hours-long infusion administration.

Our company designs and develops precision small molecules that we believe could substantially extend the lives of cancer patients who would otherwise run out of treatment options or have to cease treatment due to intolerable drug toxicity. Our lead drug candidate, which has not been approved by the US Food and Drug Administration, is TYRA-300: the first oral drug of its kind to enter the clinic. As an FGFR3-selective agent, TYRA-300 has the potential to extend the lives of patients and mitigate the common side-effects of currently marketed non-selective FGFR inhibitors, including liver damage, diarrhea, painful mouth sores, eye toxicity, skin rashes and sensitivity, hair loss, and debilitating fingernail pain and disfigurement. There are over 100,000 cancer patients in the U.S. today that could potentially benefit from TYRA-300, including approximately half of the 80,000 new bladder cancer diagnoses every year in the U.S.

This same drug candidate, TYRA-300, also shows promise in treating genetic skeletal dysplasias such as achondroplasia (dwarfism) based on pre-clinical data. Over 40,000 kids in the U.S. could potentially benefit every year from TYRA-300. Based on positive pre-clinical results,

we may decide to seek orphan designation for achondroplasia since the IRA provides an exclusion from forced negotiation/capped pricing for a drug that is orphan designated for only one rare disease or condition and that is approved for only an indication (or indications) for such disease or condition.

Whereas large molecules are typically administered intravenously by injections, most small molecules, like TYRA-300, can be administered orally as a pill. We believe TYRA-300 holds the promise of children avoiding daily injections for skeletal dysplasia and for cancer patients to be able to take a pill rather than travelling to an outpatient clinic for infusions (which can be expensive, inconvenient, and time consuming).

By establishing different periods following approval when negotiation eligibility may begin for large molecules (11 years after BLA approval) and small molecules (7 years after NDA approval), the Inflation Reduction Act disadvantages small molecules like TYRA-300.

Our largest investors are raising questions and have asked us to take into account the impact of the IRA on our clinical development timeline for TYRA-300 in certain indications. Why? Because if we were to seek and obtain approval initially for bladder cancer, this approval would trigger the 7-year price negotiation application for TYRA-300, potentially adversely impacting aggregate drug sales for skeletal dysplasias in children if an approval for this indication came after a bladder cancer indication approval, because upon approval of the second indication, less than 7 years would remain until the drug could potentially become subject to the IRA forced negotiation/capped price provision.

Conversely, if we were to seek and obtain approval initially for skeletal dysplasias, instead of bladder cancer, this approval would not trigger the 7-year rule if we receive orphan designation for this disease and come under the IRA's orphan drug exclusion, avoiding the potentially adverse impact of the 7-year timeline on aggregate drug sales for skeletal dysplasias. The 7-year clock would then start to run when we subsequently receive approval for a bladder cancer indication. In other words, because of fiduciary obligations owed to their respective investors (which include pension and retirement funds), our investors and we are being forced to consider choosing between advancing treatment for cancer patients versus progressing treatment for children with genetic disorders like skeletal dysplasias.

Here's how you could help these children *and* cancer patients. While we understand that the Centers for Medicare & Medicaid Services (CMS) is not seeking comment on Section 30.1, we respectfully urge you to please support applying to NDA-approved drugs the same 11-year period applicable to BLA-approved drugs before eligibility for the IRA's forced negotiation/capped price provision begins. Creating small- and large-molecule parity for negotiation eligibility at 11 years also would reduce the importance of the orphan drug exemption in determining whether the drug merits investment today, thereby benefitting patients through earlier access to multiple indications.

* * * * *

We appreciate you considering our comments as you develop Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented appropriately and that the potential harm to patients from fewer innovative medicines is minimized. Please contact me by telephone at (212) 574-8225 or by e-mail at afawaz@tyra.bio if you have any questions regarding our comments.

Sincerely,

A handwritten signature in black ink that reads "Ali Fawaz". The script is fluid and cursive, with the first letters of the first and last names being capitalized and prominent.

Ali D. Fawaz
General Counsel and Secretary



April 14, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Center for Medicare and Medicaid Services
Baltimore, MD 21244

Meena Seshamani, M.D., Ph.D.
Director, Center for Medicare
Center for Medicare and Medicaid Services
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Brooks-LaSure and Director Seshamani:

The U.S. Chamber of Commerce (“the Chamber”) in conjunction with the Chamber’s Global Innovation Policy Center (“GIPC”) urges the Centers for Medicare and Medicaid Services (“CMS”) to re-evaluate the approach taken in CMS’s Initial Memorandum, implementing certain provisions of the *Inflation Reduction Act* (“IRA”). The Chamber supports appropriate efforts to ensure that every American has equitable access to life-saving medicines at fair market prices, from COVID-19 vaccines to new diagnostics and therapeutics combating some of the world’s most debilitating diseases. However, we firmly believe that both the IRA itself, and the implementation contemplated by the guidance document, will harm life-science innovation and limit choices of life-saving medications for Americans.

The Chamber’s primary, although by no means exclusive or exhaustive, concerns can be summarized in three points:

1. Analysis and experience in other countries proves that market-restrictive policies like the IRA’s price controls deter future innovation, inhibit patient access, and limit patient choice;
2. The actions contemplated by the guidance document are inconsistent with the statute and would even more severely penalize life-science innovation and devalue the role of the living innovation ecosystem; and
3. Under applicable legal provisions and regulatory procedures, the Administration must solicit and then consider stakeholder feedback through a formal request for comment under the appropriate rulemaking mechanism. In addition, the guidance’s thirty-day deadline and restricted comment solicitation for only some elements of the implementation fail to give stakeholders adequate time to fully and fairly participate in the regulatory process.

The Chamber’s additional concerns are outlined in more detail below.

- I. Market-restrictive policies like the IRA’s harmful, ill-conceived price controls have a negative impact on innovation that results in restricted access to new, innovative, and life-saving medications by American patients.

In March, the Chamber released its *2023 Patient Access Report (Phase One)* (“The Report”). As GIPC recently explained in a letter to HHS Secretary Xavier Becerra, the Report confirms what proponents of the free market system already know: marketplace competition and effective intellectual property protections give patients greater access to the latest life-saving medicines.¹ In contrast, the Chamber’s research shows that market-restrictive policies like artificial price controls deter future innovation, inhibit patient access, and ultimately limit patient choice.

Reducing barriers to access has long been a health policy priority and focus for Congress and the business community. The Chamber supports appropriate, effective efforts to help mitigate and overcome obstacles to life-saving medicines. But, government price setting will create additional access challenges for Americans.

Unfortunately, many have accepted the failed premise that government intervention and price setting is the most effective way to provide patients with access to life-saving innovations. This approach is embodied within the drug pricing provisions of the IRA. While the IRA claims to promote access by controlling prices through so-called “negotiation,” the reality is that innovators are forced to comply with the government’s arbitrary and coercive price control scheme or face crippling penalties. At the same time, incentives to develop generic and biosimilar medications, one of the key components in the innovative ecosystem in today’s biopharmaceutical market, are virtually destroyed – embedding price controls in the U.S. market in a way that would be virtually irreversible for future generations of medicines.

The Chamber’s Report cautions that the IRA’s drug pricing penalties will harm patients by causing them to forfeit early and extensive access to the best life-saving medications. The Report’s methodology shows that in other OECD countries which have implemented price controls, patients see fewer overall biopharmaceutical product launches, including biologics and oncology products, and have delayed access to medicines.² For example, prior to the enactment of the IRA’s price controls, out of 104 new oncology products released globally, 80% were launched in the U.S., while only 58% were launched in Europe. Similarly, in several benchmark countries, patients can often wait up to several hundred days to receive access to life-saving treatments, waiting an average of 133 days in Germany and up to 500 days in Spain.

The IRA’s anticipated harms have already been revealed through the numerous life-science innovators who have officially ended product research and development programs, citing the new price controls. Anecdotally, for example, Eli Lilly CEO Dave Ricks said the company had already dropped a blood cancer drug from its R&D pipeline because they “couldn’t make the math work . . .

¹ Ltr from David Hirschmann, President and CEO, Global Innovation Policy Center, to Secretary Xavier Becerra, March 22, 2023.

² The report found that fewer biopharmaceutical products overall launched in Canada, Japan, South Korea, Australia, and European Union member states than in the United States over the past 20 years.

[i]n light of the Inflation Reduction Act, this program no longer met our threshold for continued investment.”³ Similarly, Novartis warned that the new law could discourage research in its most promising areas of research: RNA and radioligands.⁴ Finally, Alnylam has stopped the development of a treatment for a rare eye disease due to the need “to evaluate impact of the Inflation Reduction Act.”⁵

In addition, research by The Pharmaceutical Research and Manufacturers of America (“PhRMA”) shows the IRA’s pricing provisions may put the development of more than 400 new medicines at risk.⁶ This research indicates these potential medicines under development target some of the most common, yet serious, chronic diseases affecting America’s seniors, including Alzheimer’s, diabetes, and congestive heart failure.⁷ Unfortunately, this report, too, demonstrates the IRA’s ill-conceived price controls are already having a “chilling effect” on research and development. According to the report, life science innovators believe the IRA’s current framework will undermine advances critical to patient well-being.⁸ In fact, when asked, some 82% “or more of companies with pipeline projects in cardiovascular, mental health, neurology and cancers expect substantial impacts on R&D decisions....”⁹

These are but a few of the most prominent examples of the type of innovative, life-saving products whose realization, availability and ultimately access are ironically threatened by the IRA’s price controls to purportedly improve access. As more information comes to light, it is likely to become clear that the most vulnerable patients – including older Americans, those diagnosed with rare diseases, and underserved populations– will pay the price for innovation lost to the IRA. To describe these policies as disastrous for American innovation would be an understatement. Government intervention in the market establishment of prices undermines the innovation ecosystem that enabled the U.S. to become one of the most inventive countries in the world. Decisionmakers must consider the implications of price controls for patients before proceeding with the implementation of the IRA’s framework, which would jeopardize U.S. leadership on biopharmaceutical innovation and access to treatments. The ability of American patients to access life-saving innovations in a timely manner depends on it. Surely this outcome—less innovative medicines and longer wait times—isn’t what any policymaker or advocate wants.

- II. Actions contemplated by the guidance are not supported by the statute and further undermine life-science innovation, devalues the living innovation ecosystem, and limits patient access to new, life-saving medications.

As if the IRA’s price controls are not harmful enough to America’s life-science ecosystem, it appears that interpretations and actions contemplated by the Administration in this guidance go beyond the statutory text and further exacerbate the law’s negative effects. For example, the

³ Joe Grogan, *The Inflation Reduction Act Is Already Killing Potential Cures*, The Wall Street Journal, November 3, 2022.

⁴ Ludwig Burger, *Novartis warns U.S. plan to curb drug prices could hit key research*, Reuters, January 20, 2023.

⁵ Grogan, *supra* note 1.

⁶ Medicines in Development, 2023 Report, Pharmaceutical Research and Manufacturers Association of America.

⁷ *Id.*

⁸ *Id.*

⁹ *Id.*

proposed guidance anticipates establishing rules that would penalize life-science innovators for investing in extensive research and development to acquire patents for selected medications. Under the proposed guidance, the agency would “consider the length of the available patents...and may consider adjusting the preliminary price downward” if the patents last “for a number of years.” Given the timelines set forth in the IRA, this could include both patents on medications originally approved and patents secured for subsequent innovations.

This policy could penalize America’s life-science innovators for engaging in both initial product innovation and in the additional research and development into both new treatments and new applications of existing treatments, in a way that is inconsistent with the United States Government’s deliberate, longstanding policy decisions, on which companies and investors have relied for many years, to bolster innovation with patent protection in the U.S. Both theory and reality suggest that more patents in a therapeutic class expand innovation and economic growth, expand patient choice, and advance the public good with better health. Innovation is not a one-time, compartmentalized process. When a life sciences innovator files an initial patent claim it often does so in the early stages of research and development, years before an intended product reaches the market and all aspects of its applications and treatments have been clinically tested. Extensive clinical trials and continuing investments in research and development are required to uncover subsequent health conditions that may be treated by the initial product. The result is living innovation, a tree that continues to bear fruit. From delivery efficacy and patient compliance to dosages, mitigation of side effects, extended-release formulations, and entirely new treatments, so-called “follow-on innovations” deliver invaluable benefits to patients and consumers.¹⁰

More than 60 percent of oncology medicines approved a decade ago went on to receive additional approvals, and more than 70 percent of these additional approvals occurred seven or more years after initial approval, and as such required significant investment in research and development on the part of the innovator. These new uses provide treatment options for different diseases, including rare diseases, or additional patient populations such as children. However, with the policies laid out in the IRA guidance, instead of these critical advances, companies will have to reconsider whether post-approval research is sustainable, given the commitment of time and resources.

One product that demonstrates the value of living innovation is Botox. When Botox was initially approved, it was to treat two rare eye muscle disorders. Today, there are more than 12 approved indications, including for overactive bladder.¹¹ Similarly, AZT was originally developed as a failed attempt at cancer treatment.¹² It was only years after its failed application as a cancer treatment—and untold investments in clinical trials and research—that its potential in the fight

¹⁰ Professor Kristen Osenga, *Are “patent thickets” to blame for high drug prices*, Richmond-Times Dispatch, Nov. 30, 2022 (“It’s no secret that drug manufacturers regularly continue to innovate drugs long after they’re originally proven safe and effective. There are countless legitimate reasons to do so. Sometimes, post-market research suggests that a particular dosage or delivery method could be superior to the original.”).

¹¹ *Id.* AbbVie Inc., Press Release, AbbVie to Showcase Migraine Portfolio and Pipeline During the 16th European Headache Federation Congress (Dec. 6, 2022).

¹² Christopher M. Holman, *Why Follow-On Pharmaceutical Innovations Should Be Eligible For Patent Protection*, IP-Watch, Sep. 21, 2018, available at <https://www.ip-watch.org/2018/09/21/follow-pharmaceutical-innovations-eligible-patent-protection/>.

against HIV/AIDS was discovered.¹³ Without the ability to engage in follow-on innovation and secure patent protections, it is questionable whether the new treatments for either of these life-science innovations would be available in the future.

Each stage of innovation requires new investment and risk, which is made possible by incentives like the potential for patent protection. According to one study, the median cost of getting a new life science innovation to market was \$985 million, with an average overall cost of \$1.3 billion.¹⁴ Other studies estimate the cost, based on the amount of research and clinical trials required, could be as high as \$2.8 billion.¹⁵ The reality is that cutting-edge medical treatment is costly, and the hope it gives to patients with previously incurable diseases and illnesses is immense. To justify these substantial costs and investments, many of which never materialize or become profitable, innovators must have access to potential patent protection, and the ability to recoup significant investments to enable future innovations and follow-on uses that arise later in the product's development lifecycle.

Simply put, given the significant costs associated with bringing any iteration of a product to market, without the ability to secure full scope of protection and additional protections for follow-on innovations, life science companies will not invest in new or improved versions of their medicines. Actions contemplated by the guidance, and especially its penalization of companies that secure additional legal rights, would undermine the living life-science innovation ecosystem and prevent new medicines and treatments for existing medicines from entering the market. This would ultimately harm the very people CMS wishes to protect: American patients suffering from debilitating diseases.

To be clear, the Chamber believes that the IRA's price-control provisions are unconstitutional. But the underlying defects in the statute are no justification for CMS to go even farther in guidance and undermine innovation and patient access even more than the IRA itself requires.

- III. The thirty-day window for comments contemplated by the guidance is insufficient and provides inadequate notice, which is exacerbated by regulatory overreach in the guidance; stakeholder feedback should be solicited through formal, robust notice and comment mechanisms.

CMS's approach in implementing the negotiation provisions of the IRA exceeds CMS's statutory authority and encroaches on the authority of other parts of the Executive Branch. Specifically, in assessing whether a biosimilar or generic competitor has come to market, CMS proposes to evaluate its own prescription drug event data to determine if competition is taking place, an authority that cannot be found in the IRA. Similarly, CMS intends to conduct its own assessment of clinical value and product safety in the negotiation process, in a manner that exceeds the limited authority to consider evidence regarding alternative treatments that is set forth in the

¹³ *Id.*

¹⁴ See generally Wouters OJ, McKee M, Luyten J, *Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018*, JAMA, March 3, 2020

¹⁵ Robert Zirkelbach, *The Cost of Innovation*, PHRMA, November 19, 2014.

statute. Evaluation of competition and clinical value assessment in a comprehensive fashion are roles delegated to the FTC and FDA, respectively – not to CMS. By going beyond the statute in these areas, CMS is exceeding its authority and expertise and setting up a slippery slope with even more significant government interference in our health care system and free markets.

CMS has also been touting transparency and stakeholder engagement as CMS moves forward to implement the IRA. Unfortunately, it's not the number of meetings that matters so much as the substance of those meetings. Despite months and months of CMS effort, too many unanswered questions remain that will have significant bearing on the state of the U.S. economy and patients who rely on the Medicare program for access to needed medicines.

As a threshold matter, the Chamber notes that CMS requires stakeholders to submit their comments on the guidance within thirty days, which is half the time typically provided for public comment on initial rules for a new program. Thirty days is far too little time for stakeholders to develop meaningful input on a major new program that CMS itself has described as “novel” and “complex”, particularly given the regulatory overreach reflected in the guidance. This limited window hardly allows patients and other stakeholders to provide meaningful input and suggests that CMS is not interested in hearing from relevant parties in a manner that would shape its decisions. These issues are vitally important and deserve an opportunity for meaningful and effective comment by all interested parties.

This critical public policy matter requires a formal, robust notice and comment period. Moreover, CMS should solicit comment on all topics discussed in the Memorandum, not merely on a subset of those topics. Indeed, we recommend that CMS utilize notice and comment rulemaking to obtain public input here, given due process constraints, the Medicare statute's notice and comment requirements, and core public participation values.¹⁶ This is particularly important in light of the obvious legal and practical concerns raised by core aspects of the guidance, as well as serious legal questions about the nature and validity of the statutory provisions being implemented.

IV. Conclusion.

With the passage and implementation of the Affordable Care Act, Congress and the Obama Administration believed that access to health care services and treatments would be achieved by expanding comprehensive health coverage to all Americans. While the Chamber supports increasing the number of Americans with health coverage, we are mindful that barriers persist in a different way as higher deductibles, and out of pocket costs mitigate premium increases but also pose challenges to access. Now with the passage and implementation of the Inflation Reduction Act, it appears that Congress and the Biden Administration are focused on a new false panacea, a mistaken belief that artificially holding down prices will ensure access to therapies. However, with this new form of expanded government intrusion in our health system, our country will see that the IRA imposes new barriers to access as therapeutic pathways and research are quashed.

¹⁶ See, e.g., 42 U.S.C. § 1395hh(a)(2); *Azar v. Allina Health Servs.*, 139 S. Ct. 1804, 1808, 1815-16 (2019); *Ralls Corp. v. Comm. on Foreign Inv. in U.S.*, 758 F.3d 296, 318-19 (D.C. Cir. 2014).

The Chamber appreciates the opportunity to submit these comments for the record regarding CMS's IRA implementation guidance. We stand ready and willing to work with this Administration to find lawful and appropriate ways to ensure that life-saving medications are both available and accessible to all Americans. However, the Chamber cannot and will not support misguided, market-restrictive, and legally defective efforts that limit patient access and choice and undermine the living life-science innovation ecosystem. The Chamber strongly urges CMS to withdraw this guidance and instead engage in a formal, robust comment process that is consistent with the statute to ensure that all stakeholder voices are heard and that no adverse action is taken which will undermine American innovation.

Sincerely,



David Hirschmann
President and CEO
Global Innovation Policy Center
U.S. Chamber of Commerce



Neil Bradley
Executive Vice President, Chief Policy Officer,
and Head of Strategic Advocacy
U.S. Chamber of Commerce

Chiquita Brooks-LaSure

Administrator

Centers for Medicare & Medicaid Services

Submitted Electronically via IRAREbateandNegotiation@cms.hhs.gov

April 14, 2023

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Brooks-LaSure:

UCB is a global biopharmaceutical company with U.S. headquarters located in Atlanta, Georgia. With more than 8,700 employees globally, we are inspired by patients and driven by science. Our focus is on innovating new medicines to treat severe, chronic neurological, immunological, and rare conditions. UCB is committed to ensuring that all patients have affordable access to the right medicine at the right time, regardless of age, ethnicity, geography, or economic circumstance. Patients are at the heart of everything we do at UCB, from where we invest our research dollars to how we engage with other stakeholders to bring new therapies to market. Every day, we work to ensure that patients have the best individual experience while promoting access to high-quality, coordinated, affordable care and equitable access to medicines for *all* patients.

UCB appreciates the opportunity to provide comments to the Center for Medicare & Medicaid Services' (CMS's) Medicare Negotiation Program: Initial Memorandum (hereinafter "the Memorandum"). As a patient-centered company, UCB shares CMS's commitment to ensuring patients have affordable access to the best treatment for their individual circumstances. We offer the following comments to the Memorandum for CMS's consideration:

I. (Section 60.1) Establishment of Single Proposed Maximum Fair Price (MFP) for Negotiation Process

In the Memorandum, CMS states that it intends to base the single MFP on the cost of the selected drug per 30-day equivalent supply, weighted across dosage forms and strengths – as opposed to a per unit (e.g., tablet, capsule, injection) or a per volume or weight-based metric. UCB appreciates that CMS intends to use this approach to allow for a more direct comparison with therapeutic alternatives, which might have different dosage forms, strengths, and frequency of use than the selected drug. However, we have concerns about the use of this methodology and how it will be applied to certain treatments.

The calculation CMS outlines in the Memorandum is complicated and may not be appropriate as applied to certain treatments or types of treatments. Unclear or inconsistently applied methodology can unfairly disadvantage some therapies. While the methodology may be relatively straightforward as applied to medications for chronic conditions that are taken at regular intervals, it may prove problematic when applied

to certain products or types of products. For example, medications used at irregular dosages or intervals, such as rescue medications; medications used for multiple indications may have unclear or misleading 30-day averages; and dosing averages across formulations could have unclear or misleading 30-day averages due to different uses and sites of care.

For example, midazolam used as a rescue medication used to treat acute repetitive or cluster seizures. Rescue medication is not intended to be used daily and should not be used more than five times per month. A patient may have several cluster seizures per month necessitating use of the medication; alternatively, a patient may go for several months without experiencing a cluster seizure, therefore without the need for a dose. No two patients are affected the same way and, as such, will not have the same treatment schedule. In fact, a single patient's use of such a rescue medication may vary over the course of a lifetime. In the case of a rescue medicine intended for acute symptoms, it would be confusing and misleading to apply a single MFP across a 30-day supply as a standard 30-day supply does not exist.

Treating patients with generalized myasthenia gravis (gMG), a rare disease, who are AChR or MuSK antibody positive is complicated.¹ The recommended dose of many treatments is based on body weight tier/band associated with a fixed dose and the treatment cycle may be based on a provider observation period, or after gMG symptoms begin to worsen – which varies patient-by-patient and will vary for the same patient within a lifetime. gMG is a highly heterogeneous disease which presents differently patient-to-patient and, often, differently hour-by-hour in the same patient. Because gMG is such a diverse disease, treatment is necessarily diverse and tailored to the unique disease journey of each patient during each stage of their disease. Attempting to construct a standardized 30-day supply for such a treatment would not only be confusing but misleading.

UCB encourages CMS to work with stakeholders – including manufacturers, patient groups, and provider groups – to better understand how 30-day equivalent supplies are calculated for those medicines that have irregular or varied dosing schedules.

II. (Section 60.3.1) Identifying Therapeutic Alternatives for the Selected Drug

In the Memorandum, CMS states that, for each indication of a selected drug, it will identify a pharmaceutical therapeutic alternative(s) (covered Medicare Part D or Part B drugs or biologics only). CMS states that, in identifying therapeutic alternative(s), it will rely on data submitted by the manufacturer and the public, Food & Drug Administration (FDA) approved indications, indications included in CMS-approved Part D compendia, widely accepted clinical guidelines, and peer-reviewed studies. CMS goes on to specify that it will start with therapeutic alternatives within the same chemical or therapeutic class, or mechanisms of action, before considering other drug classes, and that, in the case of therapeutic alternatives not yet in compendia or evidence-based guidelines, it will rely on clinical evidence through literature searches. UCB requests additional clarity with respect to how CMS will identify *clinically appropriate* comparator therapeutic alternatives, particularly in the case of chronic and rare diseases.

When identifying therapeutic alternatives for selected drugs, UCB encourages CMS to incorporate the patient point of view. The value of a treatment is more than a mathematical calculation of efficacy and cost, and the value of a treatment differs according to *each specific patient* being treated. Patient perspectives provide critical insights into what is most important to patients, such as improved productivity, out-of-pocket (OOP)

¹ ClinicalTrials.gov. Accessed January 2023.



spending, ability to participate in activities of daily living, impact on caregiver burden, improvement over alternative treatments, impact on public health, and the promise of hope (among other priorities). Incorporation of patient perspectives will help to account for the nuances of different treatment's impact on the holistic patient experience and reflect individual patient viewpoints and disease journeys.

Newer, more targeted therapies bring disease control faster and more consistently without the risk of adverse effects. It is important to consider these clinical attributes when identifying a therapeutic alternative. UCB encourages CMS to select therapeutic alternatives carefully to ensure that patients are not inadvertently driven to inferior treatments – e.g., treatments that are clinically inferior or have a greater side effect profile but have a lower cost because they have been on the market for a longer time. When selecting a therapeutic alternative, CMS should rely on a variety of credible data sources that account for the diversity of patient populations, particularly data from real-world settings, and reported by patients directly. For example, real-world evidence (RWE) can provide insight into the benefit of a treatment and its usage in a real-world scenario, beyond data collected in randomized clinical trials (RCT).

When selecting a treatment alternative, UCB encourages CMS to consider unmet need and improvement over existing treatments from the patient perspective. Below, please find disease-specific examples to illustrate the importance of considering the nuance among a patient population and the heterogeneity of disease when selecting a treatment alternative. Additionally, when considering the improvement of a treatment over existing therapies, UCB encourages CMS to also consider the additional burden that certain older formulations – e.g., requiring multiple infusions – may place on patients and families further highlighting the need for additional treatment options and formulations.

A. Treatment of Seizure Clusters

Seizure clusters, also known as acute repetitive seizures, describe a pattern of increased seizure frequency or severity which is recognizable to the patient and/or caregiver, and which is not the patient's usual seizure pattern. Patients experiencing seizure clusters have been shown to have higher death rates, and the occurrence of frequent seizures in short periods of time is associated with an increased incidence of post-ictal psychosis.² Patients with clusters are more frequently transported to emergency departments (ED) and have more hospital admissions. Use of a rescue medication that may stop or prevent the evolution of seizure clusters at home, school, or work may prevent transport to the ED or hospital admission and lessen stress for the patient, family, and caregivers.³

NAYZILAM® (midazolam), is a prescription nasal spray used for the short-term treatment of seizure clusters in patients 12 years of age and older. While, prior to approval of NAYZILAM®, other rescue treatments were available, NAYZILAM® addressed an unmet need for this population and represents a significant improvement over previously available treatment. The previously approved rescue treatment for seizure clusters was a rectal gel; the nasal spray route of administration represents a significant improvement for this patient population.

² Post-ictal psychosis (PIP) is a severe mental condition associated with epilepsy, characterized by a disconnection from reality.

³ See Patricia Penovich, MD, EFMN. Acute Repetitive Seizures (ARS) or Cluster Seizures. Jan. 2020. [Acute Repetitive Seizures \(ARS\) or Cluster Seizures - \(epilepsyfoundationmn.org\)](https://www.epilepsyfoundationmn.org/ARS-or-Cluster-Seizures).



B. *Myasthenia Gravis is a “Snowflake” Rare Disease*

Generalized myasthenia gravis (gMG) is an extremely heterogeneous disease, varying not just patient-to-patient but hour-to-hour within a single patient. The nature of the disease further complicates the already complex world of rare disease and the subjective nature of the treatment approaches from physician-to-physician and patient-to-patient. Newer, more targeted therapies and solutions meet the unique needs of gMG patients and providers, while older, less innovative therapies may fall short in treating the disease and slowing its progression. Because gMG is a rare disease with limited treatment options available, it is imperative that CMS fully and carefully consider patient perspectives and utilize RWE to account for the true lived patient experience, which includes the social, psychological, and emotional effects of living with the unpredictability of a disease which is often not visible to others – including healthcare providers.

In the case of gMG treatments, conventional therapies are associated with side effects, treatment-related comorbidities, and long-term toxicities that can prevent those treatments from being suitable maintenance therapies. Additionally, conventional therapies may expose patients to disease exacerbations and poor quality of life – e.g., osteoporosis-related fractures, psychiatric disorders, renal failure, thrombotic events, aseptic necrosis, infection and gastrointestinal bleeding. Additionally, clinical effectiveness of “standard of care” or “best practice” therapy is limited and there is wide variability with respect to onset of action, patient response, and health outcomes.

UCB urges CMS to take into account the nuances of treatment and avoid generalizing that all patients will have the same response to “standard of care” treatment. Any consideration of alternative treatments for gMG must recognize the heterogeneity of the disease and focus on a treatment’s impact in the subset of patients with inadequate disease control despite being on standard of care therapy. Considering that many patient populations are very heterogeneous, and the effectiveness of a treatment is not equivalent across a population, UCB encourages CMS to engage with disease-specific organizations and providers, utilizing treatment guidelines, when evaluating a clinically appropriate “treatment alternative”.

Access to *the most clinically appropriate* treatment is highly important for gMG patients as uncontrolled gMG leads to crisis, exacerbations, and decreased patient quality of life. For example, over a one-year period, refractory patients had a significantly greater chance of:

- a. Having at least one myasthenic crisis (21.3%), compared with non-refractory patients (6.1%, $p<0.001$);
- b. Having at least one exacerbation (71.2%), compared with non-refractory patients (32.4%, $p<0.001$); and
- c. Hospitalization and/or have an emergency department visit compared with non-refractory patients and non-MG control patients ($p<0.001$ for all).

C. *Newer Rheumatoid Arthritis Treatments Demonstrate Superior Clinical Benefit*

Rheumatoid arthritis (RA) is a chronic inflammatory disorder that can damage a wide variety of body systems, including the skin, eyes, lungs, heart, and blood vessels. Unlike the wear-and-tear damage of osteoarthritis, RA affects the lining of the patient’s joints, causing painful swelling that can eventually result in bone erosion and joint deformity. The inflammation associated with RA can damage other parts of the body as well. New



types of medications have dramatically improved treatment options. However, RA can still cause physical disability.⁴

Without appropriate treatment, RA inevitably causes irreversible damage to the structural joints and is often accompanied by multiple organ damage. Joint damage progresses in the early stages after onset, and the deformed joints cause irreversible physical dysfunction. Prompt diagnosis along with appropriate treatment is essential for the clinical management of RA. Treatment options for RA have improved significantly in the 21st Century and now include medications that slow the progression of joint damage. These drugs are called disease-modifying antirheumatic drugs (DMARDs). These drugs act on the immune system to slow the progression of RA. The aim of treatment is to lower disease activity or achieve remission.

When a patient is initially diagnosed with RA, they are usually prescribed *methotrexate* (MTX). MTX is a synthetic DMARD (csDMARD) that reduces inflammation via multiple mechanisms. It is usually combined with a glucocorticoid (GC) drug such as *prednisone* (*Deltasone*). MTX is used as an anchor DMARD in treating RA and many patients benefit from MTX; however, a large number of RA patients suffer from side effects. A variety of side effects can be associated with MTX when treating RA patients, from mild to severe or discontinuation of the treatment.⁵

Biological DMARDs (bDMARDs), which are made from living organisms or contain components of living organisms, target TNF, IL-6 receptors and others; and targeted synthetic DMARDs (tsDMARDs), such as Janus kinase (JAK) inhibitors, have been introduced in addition to conventional synthetic DMARDs (csDMARDs), such as MTX. Since the introduction of these treatments, clinical remission has become a realistic therapeutic goal for the majority of RA patients. Sustained remission facilitates prevention of structural joint damage over a long period of time, in addition to preventing progression of physical dysfunction.^{6,7}

RA does not present or progress the same for every patient; different treatments are more effective for different patients, and it may be difficult to figure out which medication (or combination of medications) will work best to help a patient regain control of their RA. It is very important that these patients have access to the best and most medically appropriate treatment for their specific circumstances.

III. (Section 110) Part D Formulary Inclusion of Selected Drugs

In the initial Memorandum, CMS reiterates that Medicare Part D plans must include each covered Part D drug that is a selected drug on Part D formularies. However, like the IRA statutory language, the Memorandum does not contain any additional parameters Part D plans must follow with respect to selected drugs. Under the redesigned benefit, plans will have a significant increase in financial liability. Considering this dynamic, plans may apply burdensome utilization management, making it difficult for patients to access certain therapies. Additionally, because plans are required to cover negotiated products, it is unlikely that plans will obtain high rebates on those products, incentivizing plans to prefer non-negotiated drugs from which they can obtain high

⁴ See Mayo Clinic. Rheumatoid Arthritis: symptoms and causes.

⁵ Wang W, Zhou H, Liu L. Side effects of methotrexate therapy for rheumatoid arthritis: A systematic review. *Eur J Med Chem*. 2018 Oct 5;158:502-516. doi: 10.1016/j.ejmech.2018.09.027. Epub 2018 Sep 13. PMID: 30243154.

⁶ Yoshiya Tanaka, Recent progress in treatments of rheumatoid arthritis: an overview of developments in biologics and small molecules, and remaining unmet needs, *Rheumatology*, Volume 60, Issue Supplement_6, November 2021, Pages vi12–vi20, <https://doi.org/10.1093/rheumatology/keab609>.

⁷ Methotrexate vs. biologics – which is more effective as a first-line treatment? *Annals of Rheumatic Disease*. Jun 14 2019.



rebates. UCB is concerned with potential unintended consequences that may result from the IRA's drug pricing provisions – namely, that gains in affordability may come at the expense of access.

Unnecessarily Restrictive Utilization Management Harms Patients. Utilization management (UM) is now an integral part of most public and private health plans. The great majority of Americans are now enrolled in privately or publicly funded health plans that use UM programs as a primary cost-containment strategy. This includes 90 percent of privately insured employees and all Medicare and Medicaid participants.⁸ Utilization management for the sole purpose of reducing cost can interfere with early intervention and result in more costly procedures down the road due to a delay in care.⁹

Also known as “fail first,” step therapy is a tool used by health plans to control costs. Under its rules, patients are required to try one or more alternative prescription drugs, chosen by their health plans, before coverage is granted for the drug originally prescribed by a patient's health care provider. Step therapy is applied to medications treating a range of diseases and conditions including epilepsy, autoimmune diseases, psoriatic and rheumatoid arthritis, cancer, diabetes, multiple sclerosis, mental health, and many, many others. Its negative effects can include far worse than delays in treatment; it can give a serious disorder more time to progress, often causing significant anguish for the patient, as well as increasing the burdens on health care providers and, thus, increasing costs – both to the patient and, ironically, the insurance company. In the case of epilepsy, the practice can even precipitate Sudden Unexplained Death in Epilepsy (SUDEP), due to higher instances of SUDEP in patients with uncontrolled seizures.¹⁰

While the medications beneficiaries are forced to “step through” may lead to near-term savings for plans, such forced substitutions can also yield adverse clinical effects and/or suboptimal clinical outcomes for patients. As a result, such policies often lead to increased costs in the long run. Step therapy policies prioritize the short-term cost considerations of health plans above care-based decisions made within the patient-provider relationship.¹¹ UCB would like to offer disease-specific examples of how unnecessarily restrictive step therapy protocols can harm patients.

a. *Epilepsy*

Insurance companies are increasingly forcing epilepsy patients to try other treatments before covering the cost of originally prescribed treatments. This jeopardizes those patients' ability to drive and can even put their employment at risk. The majority of patients with epilepsy can control their seizures and other symptoms through proper drug treatment.¹² However, when patients are restricted from accessing the treatment(s) prescribed by their physician, they have a high risk of experiencing sudden seizures and other complications. Patients treating epilepsy can be particularly susceptible to adverse reactions from medications that differ from the treatments their doctors prescribe. Forcing epilepsy patients to step through other

⁸ [Utilization Management as a Cost-Containment Strategy \(cms.gov\)](https://www.cms.gov/medicare/coverage/determinationprocess/coverage-determinations/coverage-determinations-2019/coverage-determinations-2019-01-01-2019-01-01)

⁹ See generally: Boytsov, Natalie, et al. Impact of Plan-Level Access Restrictions on Effectiveness of Biologics Among Patients with Rheumatoid or Psoriatic Arthritis. June 2019. <https://doi.org/10.1007/s41669-019-0152-1>.

Avalere. Step Therapy Can Lead to Higher OOP Costs for Crohn's Disease Patients. Oct. 2020.

Thomson Reuters. Thomson Reuters Study Finds Step Therapy Programs May Increase Overall Healthcare Costs for Employers. Media Release: 30 Mar 2009.

¹⁰ See Epilepsy Foundation. [Preventing SUDEP | Epilepsy Foundation](https://www.epilepsy.com/learn-more/sudep).

¹¹ Jennifer Snow, MPH; Madelaine A. Feldman, MD, FACR; Jenna Kappel, MPH, MA. ["The Impact of Step-Therapy Policies on Patients."](#) December 2019. A white paper published by Xcenda, an AmerisourceBergen company.

¹² See James Tao, MD, PhD. New treatment options for people with drug resistant epilepsy. Dec 2022.

medications before accessing the originally prescribed treatment puts many patients at risk of severe reactions.¹³

Delaying epilepsy patients access to prescribed treatments can have significant consequences, beyond simply putting those patients at risk of adverse reaction and exacerbating the severity of their symptoms. Individuals with uncontrolled epilepsy are at increased risk of losing their driver's license, their professional certifications, or potentially even their jobs. Any cost-savings gained imposing step therapy may well be mitigated by the additional costs incurred by patients who fail on the insurer's preferred medication.

b. *Rheumatoid Arthritis*

Rheumatoid arthritis (RA) is a chronic, debilitating disease that significantly impacts patients' quality of life and socioeconomic productivity. On a personal level, RA has a significant socioeconomic impact on patients' lives, and is ranked among the highest of all chronic diseases for its effects on health-related quality of life (HRQoL); limitations in physical function, as well as increased pain and fatigue affect patients' attendance at paid work, their work performance within and outside the home, and their participation in family, social, and leisure activities. Newer, more effective treatments, such as tumor necrosis factor (TNF) inhibitors, improve the signs and symptoms of disease, inhibit progression of joint damage, and improve physical function and HRQoL.¹⁴ Treatment is often able to limit or reduce joint damage and improve patients' quality of life; adhering to a treatment plan can make a big difference in patients' disease progression.

It is imperative that RA patients work with their physician to find an appropriate treatment regimen as soon as possible after diagnosis and adhere to that treatment regimen. Early diagnosis and proper treatment strongly affect patients' quality of life. In the early phase of the disease, effective treatment and strict monitoring can help to achieve remission within the shortest period. Delay in appropriate treatment can result in loss of the golden time when effective treatment must start.¹⁵

Forcing patients to step through other medications before they are able to access the treatment originally prescribed by their physician – particularly where the physician has no mechanism by which to override step therapy protocols – is inappropriate and can disproportionately negatively impact the health, well-being, and disease progression of RA patients. RA is a serious, debilitating disease and every day that RA patients do not get relief is a day spent suffering through long-term harm to their body. Delays in symptom and disease relief can result in serious complications and the need for more invasive and costly interventions like surgery and hospitalization.

What works for patient A might not necessarily be right for patient B, which is why it is important to work closely with a rheumatologist to determine the most effective treatment regimen. It can take time – sometimes a few months – to determine whether a treatment is working which can cause a long delay in patients accessing the most appropriate treatment when forced to step through other medicines. Importantly, once an RA patient switches treatments, there is no guarantee the original treatment will work as well as it once did when the patient switches back.

¹³ See Mandy Bianchi. Epilepsy patients at risk by insurer's step therapy. Dec 2017.

¹⁴ Strand V, Khanna D. The impact of rheumatoid arthritis and treatment on patients' lives. Clin Exp Rheumatol. 2010 May-Jun;28(3 Suppl 59):S32-40. Epub 2010 Jun 22. PMID: 20576223.

¹⁵ Saad, S.A., Alhaj, N.K. Delay in referral of rheumatoid arthritis patients to rheumatology clinic. *Egypt Rheumatol Rehabil* 47, 12 (2020). <https://doi.org/10.1186/s43166-020-00012-7>.



IRA Part D Redesign Incentivizes Increased Use of Utilization Management. Beginning in 2024, Medicare beneficiaries will have \$0 cost-sharing in the catastrophic phase and the income threshold for full eligibility under the low-income subsidy (LIS) program will be expanded. Beginning in 2025, the IRA makes additional changes to the Part D program. The coverage gap will be eliminated, and beneficiaries' annual out-of-pocket (OOP) costs will be capped at \$2,000 (adjusted annually for inflation) and beneficiaries will be allowed to "smooth" cost-sharing over a certain threshold across the coverage year. The government's responsibility in the catastrophic phase will be reduced from 80% to 20% and health insurance plans' liability significantly increases from 15% in the initial coverage phase to 60% in the catastrophic phase – in both LIS and non-LIS. Lastly, a new drug manufacturer discount program will require discounted prices for patients in the initial coverage phase (10%) and the catastrophic phase (20%) – in both LIS and non-LIS, with negotiated drugs excluded.

Changes to the Part D benefit do make improvements for patient affordability; however, that affordability may come at the expense of patient access to a wide range of prescription drugs. The increase in liability for health insurance plans, particularly in the catastrophic phase, may incentivize plans to increase the use of utilization management, restricting access to new, innovative treatments which often achieve better health outcomes and lead to lower overall costs to the system. Health plans are incentivized to forgo optimal patient outcomes in order to increase their bottom line. Increase in use of UM will only exacerbate the existing negative impacts of step therapy to patients. Without restrictions on plans' use of UM, patients may experience access barriers to needed therapies. As such, UCB encourages CMS to issue additional guidance, putting parameters around plans' ability to use UM tools to ensure that Medicare patients continue to have access to the most appropriate treatment for their unique circumstances.

c. Psoriasis

Psoriasis is an autoimmune disease characterized by raised areas of abnormal skin. These areas are red, pink, or purple, dry, itchy, and scaly. Psoriasis is associated with an increased risk of psoriatic arthritis, lymphomas, cardiovascular disease, Crohn's disease, and depression. There is no known cure for psoriasis, but various treatments can help control the symptoms. These treatments include steroid creams, vitamin D₃ cream, immunosuppressive drugs – such as methotrexate (MTX) – and biologic therapies targeting specific immunologic pathways. Psoriasis treatments are not all equal; different treatments are appropriate for different patients based on the degree of psoriasis and psoriatic disease severity.¹⁶ For example, systemic treatments, such as MTX, are used in patients that are not responsive to or unable to tolerate topical treatments. Biologics targeting Th1/Th17 cytokines have revolutionized psoriasis treatment.¹⁷ Studies show that the biologics approved to treat psoriasis and psoriatic arthritis can be very effective. For many people with moderate-to-severe psoriasis or psoriatic arthritis, a biologic may offer the most effective treatment available.¹⁸ Additionally, the use of a single drug or single therapy method may not work for every psoriasis patient; many patients are prescribed and find success with a combination approach to treatment. A combination approach has three main benefits: it decreases the possibility of reaching toxic levels with a single drug; the individual drugs can be prescribed at a lower dose; and a combination approach can be more

¹⁶ See National Psoriasis Foundation. www.psoriasis.org.

¹⁷ Psoriasis (Auckl). 2022 Jul 1;12:187-188. doi: 10.2147/PTT.S380486. eCollection 2022.PMID: 35801229.

¹⁸ See American Academy of Dermatology Association. [Psoriasis treatment: Biologics \(aad.org\)](https://www.aad.org/psoriasis-treatment/biologics).

¹⁸ See mayoclinic.org/diseases-conditions/psoriasis/diagnosis-treatment/drc-20355845



successful than a single treatment option.¹⁹ Psoriasis is associated with an increased risk of psoriatic arthritis, lymphomas, cardiovascular disease, Crohn's disease, and depression. As such, it is imperative that psoriasis patients have access to the most appropriate treatment for their specific disease state, without delay.

IV. Conclusion

UCB appreciates the opportunity to comment on CMS's Medicare Negotiation Program: Initial Memorandum. We welcome further discussion and look forward to working with CMS to continue improving quality of care and affordable access for all patients. Please direct any questions to Amanda Ledford, Director of U.S. Public Policy, via email at Amanda.Ledford@ucb.com or by phone at (202) 893-6194.

Sincerely,

A handwritten signature in black ink, appearing to read "Patricia A. Fritz". The signature is stylized with a large initial "P" and a long, sweeping underline.

Patricia A. Fritz

Vice President, US Corporate Affairs

UCB, Inc.

April 14, 2023

BY ELECTRONIC MAIL (IRAREbateandNegotiation@cms.hhs.gov)

Dr. Meena Seshamani
Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program Guidance

Dear Dr. Seshamani:

United Therapeutics Corporation (“United Therapeutics”) is a biotechnology company focused on the development of unique therapies and manufactured organs to address the unmet medical needs of patients with rare chronic and life-threatening conditions. United Therapeutics offers several medicines to treat pulmonary arterial hypertension (“PAH”), a life-threatening orphan disease, and also offers an oncology therapy approved for the treatment of high-risk pediatric neuroblastoma. It has also developed and commercializes the only FDA approved therapy for treatment of a rare condition known as pulmonary hypertension associated with interstitial lung disease. Longer-term, the company is actively developing technologies to solve the acute shortage of transplantable organs, through ex vivo lung perfusion, xenotransplantation, regenerative medicine, and 3D organ bioprinting.

We appreciate the opportunity to submit comments on the Centers for Medicare & Medicaid Service (“CMS”) Medicare Drug Price Negotiation Program Initial Memorandum¹ (“Initial Memorandum”) for initial price applicability year 2026 regarding the implementation of Sections 1191 through 1198 of the Social Security Act, as added by Sections 11001 and 1102 of the Inflation Reduction Act² (“IRA”). Also, we respectfully request that CMS promptly publish all submitted comments.

The U.S. pharmaceutical industry has long been a motor of innovation that provides life-saving therapies. Indeed, our company is a prime example of how entrepreneurship can thrive in a free-market economy, resulting in treatments that otherwise would never have become available.

¹ CMS, Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (Mar. 15, 2023), available at <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>.

² P.L. 117-169.

United Therapeutics CEO Martine Rothblatt founded the company in 1996, after her daughter was diagnosed with PAH. Since its founding, United Therapeutics has commercialized multiple PAH therapies based on the active ingredient treprostinil that would not exist today, without Dr. Rothblatt's leadership. The company also developed and launched tadalafil, the active ingredient in Cialis, for the orphan PAH indication, allowing this molecule to benefit PAH patients alongside its more widespread indication.

Today, United Therapeutics is a public benefit corporation with approximately 1,000 employees primarily located in the United States, and continues its commitment to patients in the areas of lung disease and organ manufacturing. The United Therapeutics success story was only possible in an environment that rewards investment, innovation, and initiative. Without such rewards, innovators and leaders will not be able to assume the risks associated with pioneering new therapies, particularly in the orphan disease space.

And yet, these foundations of U.S. pharmaceutical innovation are under threat. The IRA's capped price and forced negotiation provisions mark the most significant change to the federal healthcare programs since their enactment more than 30 years ago, signaling a shift away from the free market approach to government price controls. But in creating the drug price negotiation program, Congress set carefully defined boundaries—the IRA's goal is clear: to subject only a specified number of single source drugs to price caps, not drugs for which there are generics or biosimilars. Unfortunately, the Initial Memorandum would impermissibly expand the IRA's scope, hurting innovation by eliminating the economic incentives that are essential to the functioning of the free market pharmaceutical economy. Some of the approaches CMS has adopted could produce procedurally deficient, arbitrary, and capricious decisions in particular factual scenarios where the agency is acting beyond its limited grant of authority, lacks sufficient information to act in a non-arbitrary fashion, or has failed to fully understand or appreciate the underlying record.

As we describe in further detail below, two particularly bald examples of ways in which CMS is proposing to impermissibly expand the scope of the IRA's statutory negotiation program would be (1) expanding the number of drugs subject to forced negotiations and price caps in 2026 beyond the number clearly intended by congress and outlined in the IRA itself (ten Part D drugs) by defining the operative term, Qualifying Single Source Drug ("QSSD") so broadly as to encompass a potentially large number of different therapies, and (2) imposing an impermissibly high bar before recognizing that a generic or biosimilar is being marketed.

The Initial Memorandum is also troubling procedurally. CMS may believe that the IRA did not require formal notice and comment rulemaking in the initial years following its enactment, which is why CMS is issuing one of the most significant portions of the Initial Memorandum in final form, namely the QSSD definition and related provisions (Section 30). However, CMS should still solicit and respond to comments on this topic. Indeed, such comments may identify significant shortfalls in CMS's plans that, if implemented as described, would deprive the regulated community of constitutionally required process.

The risk of damaging the U.S. biopharmaceutical industry through poorly-considered policy choices that go beyond what Congress intended is very real. Soliciting comments is an important first step, but CMS must do more—it must carefully consider manufacturer input: CMS is

becoming an industry participant and should avail itself of the knowledge and experience that only stakeholders can provide as the agency assumes the novel role of negotiating the price for pharmaceuticals on which many patients rely.

For example, CMS overlooked an important consequence of adopting an overly broad QSSD definition (and one that is clearly inconsistent with Congressional intent). By drawing in both Medicare Part D and Part B drugs if they share the same active moiety/active ingredient and are approved for the same manufacturer, any Maximum Fair Price (“MFP”) that applies to such a QSSD in 2026 will be used to set the Part B reimbursement rate pursuant to an IRA statutory requirement³—thus subjecting Part B drugs to an MFP in 2026, which the IRA contemplates for 2028, not for prior years. The QSSD definition, as proposed, thus directly violates the letter of the IRA. CMS can and should address these and other shortcomings of the Initial Memorandum and should abandon its assertion that its solicitation of comments is voluntary and that the agency will not entertain comments to Section 30 of the Initial Memorandum.

Our comments are addressed in further detail below. In addition, United Therapeutics subscribes to the comments regarding this Initial Memorandum that are submitted by the Biotechnology Innovation Organization (BIO).

I. THE PROPOSED QSSD DEFINITION VIOLATES THE LETTER AND INTENT OF THE IRA.

In the Initial Memorandum, CMS proposes to define QSSD as follows:⁴

- For drug products, CMS proposes to treat as a single QSSD all dosage forms and strengths of the drug that have the same active moiety and are approved under New Drug Applications (“NDAs”) held by the same manufacturer.
- For biological products, CMS proposes to treat as a single QSSD all dosage forms and strengths of the biological product that have the same active ingredient and are approved under Biologics License Applications (“BLAs”) held by the same manufacturer.

This definition ignores different approvals by the U.S. Food and Drug Administration (“FDA”) and is impermissibly broad in other ways. In keeping with the IRA, CMS should define a QSSD as corresponding to a particular FDA approval.

A. The proposed QSSD definition subjects Part B drugs to the MFP in 2026, in direct violation of the IRA.

The proposed QSSD definition would sweep in both Part D and Part B drugs, which would result in the MFP setting the Part B reimbursement rate for Initial Price Applicability Year (“IPAY”) 2026, a clear violation of the IRA, which expressly limits the forced negotiation and capped

³ IRA § 1198(b)(1)(A).

⁴ IRA § 1192(e)(1); Initial Memorandum Section 30.1.

price provision to Part D drugs for 2026 and 2027, and includes Part B drugs only beginning with IPAY 2028.

As proposed, the QSSD definition would sweep in different drugs with the same active moiety or different biologics with the same active ingredient, regardless whether these drugs or products are payable under Part D or Part B. For example, a manufacturer holds two NDAs for two drugs with the same active moiety, with one drug being self-administered and therefore reimbursed under Medicare Part D, and the other being physician-administered and therefore reimbursed under Part B. If this single QSSD is subject to an MFP in IPAY 2026, the Part B drug's Part B reimbursement rate would be set at 106% of MFP, not of Average Sales Price ("ASP").⁵ Congress specifically delayed negotiation for Part B drug prices until IPAY 2028, yet CMS' overly broad QSSD definition, focusing on active moiety or active ingredient, would subject Part B drugs to an MFP in IPAY 2026.

CMS appears not to have appreciated the interplay between its overly broad QSSD definition and IRA § 1198(b)(1)(A), a prime example for why CMS must solicit and consider comments to all sections of the Initial Memorandum. As it stands, the Initial Memorandum's discussion of the negotiation factors in Section 60 or of the negotiation process addresses only Part D-related considerations. The agency also does not address the dislocations that would occur if the Part B payment rate of a drug⁶ is severely depressed by reference to an MFP negotiated solely in consideration of the Part D market.

If CMS adopted its proposed QSSD definition, it would do so in violation of the IRA and to the detriment of Part B patients. CMS must revise its QSSD definition to align with the IRA statutory scheme, which clearly contemplates a QSSD definition that focuses on the FDA approval or licensure. Such an appropriately delineated QSSD definition would avoid the unintended consequence of subjecting Part B drugs to forced negotiations and price caps prior to IPAY 2028.

B. The proposed QSSD definition would subject newly-approved drugs to negotiation, contrary to Congressional intent.

One important safeguard that Congress included in the IRA is the protection from forced negotiation and government price controls for drugs that are recently approved. The earliest an NDA-approved drug becomes eligible for negotiation is 7 years after approval, and for biologics, 11 years after BLA approval. But the overly-broad QSSD definition would include drugs with different FDA approvals and approval dates, and the Initial Memorandum would start the 7 or 11-year clock on the approval date of the first approval associated with the QSSD. For example, if a manufacturer has an NDA approved for an active moiety in 2005 and a second NDA for the same active moiety approved in 2022, CMS would treat both products as the same QSSD, and

⁵ IRA § 1198(b)(1)(A) requires amending § 1847A(b)(1)(B) of the Social Security Act (42 U.S.C. 1395w-3a(b)(1)(B)) to include that where a drug is selected and thus subject to an MFP, that drug's Part B payment is based on MFP + 6% rather than the typical ASP + 6%.

⁶ For brevity, we refer to both drugs and biologics as drugs.

would start the 7 year clock in 2005. Although approved less than 7 years ago, the 2022 NDA would be subject to negotiation.

But CMS goes further. Section 60.5.1 of the Initial Memorandum contemplates a situation where a manufacturer of a selected drug receives a new NDA or BLA, and CMS proposes to subject that newly approved product, with its own new FDA approval, to the existing MFP. Both the proposed QSSD definition and Section 60.5.1 eliminate the manufacturer's opportunity to receive a return on the investment necessary to obtain the new FDA approval. Without such compensation, manufacturers will not have the ability to innovate their existing drugs, and to generate patient benefit from existing active moieties or active ingredients. This result is particularly insidious in the context of small molecules, as the active moiety definition cuts across different active ingredients, and thus potentially across very different drugs. As noted in the introduction, United Therapeutics obtained approval for tadalafil in the PAH orphan indication. The Initial Memorandum threatens these successes and thus patient access to therapeutic innovations.

CMS's approach overrides the FDA approval scheme, which is predicated on providing patent protection and exclusivity as an incentive for pursuing a costly and burdensome FDA approval. The unintended consequence of CMS's overreach would be to stifle pharmaceutical innovation, as manufacturers will not be able to justify shouldering the significant economic burdens and assuming the risk of failure inherent in seeking a new FDA approval if the economic incentives, in the form of patent protection and exclusivity, have been severely curtailed, if not obliterated.

We urge CMS to adopt a QSSD definition that focuses on FDA approval. That would eliminate the injustice of attributing the approval date of one FDA approval to a completely distinct, different FDA approval. But if CMS retains the proposed QSSD definition, then at a minimum, CMS should commence the 7- or 11-year clock not on the date of the first FDA approval associated with the QSSD, but on the date of the most recent FDA approval. Similarly, if an MFP is in place, related products approved after the price becomes effective should not be subject to the MFP. While this approach would not address the other problems caused by the overly broad QSSD definition, it at least would preserve the incentive for manufacturers to maximize the uses and therapeutic potential of already-approved active moieties and active ingredients and to continue to innovate exiting drugs.

C. The proposed QSSD definition renders meaningless the IRA's limitation of 10 selected drugs for IPAY 2026.

A key boundary that Congress included in the IRA is the limited number of drugs subject to negotiation in the first IPAYs. For 2026, the IRA provides that only 10 drugs are to be selected, followed by 15 drugs in each of the next two years, and continuing with 20 drugs each year thereafter. Congress intentionally chose these numbers and the gradual increase after considerable debate, as evidenced by the legislative history of the IRA, going back to H.R. 3.⁷

⁷ H.R.3 - 116th Congress (2019-2020): Elijah E. Cummings Lower Drug Costs Now Act, H.R.3, 116th Cong. (2020), <https://www.congress.gov/bill/116th-congress/house-bill/3>.

CMS's broad QSSD definition referencing active moiety (for drugs) or active ingredient (for biologics) vitiates Congress's carefully constructed scheme by pressing a potentially large number of very different products into each of the 10 selected drug slots. CMS should adhere to Congressional intent and abandon its overly expansive definition of QSSD in favor of a definition that focuses on FDA approval.

D. The proposed QSSD definition is inconsistent with the long-standing federal regulatory scheme governing drug and biologic approvals.

The IRA contemplates that CMS will negotiate the prices of drugs or biologics. A plain reading of the words of the IRA makes clear that active moieties and active ingredients are simply not drugs. The IRA focuses on the price available to Medicare beneficiaries, and there are no market prices for active moieties or active ingredients for patients. Further, the IRA QSSD definition refers to drugs as approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act and marketed pursuant to such approval, and to biological products as licensed under section 351(a) of the Public Health Service Act and marketed pursuant to such licensure.⁸ The reference to the specific FDA approval is instructive; nothing in the IRA contemplates an active moiety or active ingredient as being considered the “drug.”

Yet the proposed QSSD definition would ignore the IRA's explicit references to FDA approvals. Detailed legal standards govern when different FDA approvals are required, and these are relevant to the scope of the QSSD definition. The IRA refers to “such approvals” when describing drugs subject to negotiation—and CMS should ensure consistency throughout the federal regulatory scheme by adopting FDA approval/licensure as the basis for defining a QSSD.

The IRA QSSD definition further refers to covered Part D drugs and drugs or biological products for which payment may be made under Part B. Neither the Medicare Part D nor Part B benefit provides payment for active moieties or active ingredients; rather these programs cover drugs. Among other things, this is evidenced by how CMS itself reimburses under Part B—on the basis of billing codes established for each different FDA approval. Similarly, in the Medicaid context, CMS has stated that baseline price reporting data follow the FDA approval. CMS's proposed QSSD definition is a power grab in contravention of the plain meaning of the law. The statute empowers CMS to negotiate the prices of a limited number of drugs, and CMS should abide by this mandate.

CMS is also seemingly misapplying the IRA's data aggregation provision. For purposes of determining negotiation eligible drugs, the IRA permits CMS to aggregate expense data “across dosage forms and strengths *of the drug*” in order to calculate expenditures for QSSDs to determine if a QSSD is negotiation-eligible.⁹ But this IRA provision is limited to establishing the ranking of QSSDs. And while the statutory language allows aggregation across dosage forms and strengths, and even new formulations, nothing suggests that Congress contemplated broad aggregation on the basis of active moiety or active ingredient and across FDA approvals. Further, the aggregation provision is limited to particular circumstances. Reading it as

⁸ IRA § 1192(e)(1).

⁹ IRA § 1192(d)(3)(B) (emphasis added).

supporting a QSSD definition that ignores different FDA approvals is not borne out by the statutory language.

CMS should give effect to the plain meaning of the IRA, which calls for defining a QSSD by reference to its FDA approval—not on active moiety or active ingredient.

E. The proposed QSSD definition impermissibly limits the IRA’s orphan drug exclusion, in contravention of the IRA.

CMS uses the overly broad scope of its own QSSD definition to narrow the IRA’s orphan drug exclusion. The IRA excludes from the QSSD definition a drug if it “is designated as a drug for only one rare disease or condition under section 526 of the Federal Food, Drug, and Cosmetic Act and for which the only approved indication (or indications) is for such disease or condition.”¹⁰ Yet the Initial Memorandum states that “[i]n order to qualify for the orphan drug exclusion, all dosage forms and strengths and different formulations of the qualifying single source drug ...must meet the criteria for exclusion.”¹¹ In other words, a QSSD under CMS’s reading—which includes an assembly of different products and FDA approvals—only satisfies the orphan drug exclusion if all the various products are designated for “only one” rare disease or condition, and if all the various products are only approved for indications for that one rare disease or condition.

This is not what the IRA statutory scheme contemplates and will be a disincentive to the development of orphan drugs. The following example illustrates CMS’s impermissible narrowing of the IRA’s orphan drug exclusion. The manufacturer has three NDAs, each for a different active ingredient, but all three different active ingredients share the same active moiety. Under CMS’s QSSD definition, all of these distinct products would constitute a single QSSD. The active ingredient associated with the first NDA is orphan designated for a rare disease, and the FDA approval is for an indication for such rare disease. The other two active ingredients do not have orphan designation. Under the Initial Memorandum, the QSSD would not qualify for the orphan drug exclusion. But under the plain reading of the IRA, each of the three NDAs would constitute a separate QSSD—and the first of these three QSSDs would qualify for the orphan drug exclusion, by virtue of being designated for a rare disease and FDA approved for an indication for such rare disease. This is the outcome Congress intended.

The overly-broad QSSD definition espoused by CMS contravenes the language of the IRA and the intent of Congress to incentivize orphan drug development by excepting orphan drugs from the forced negotiation and capped price provisions. This agency overreach is threatening patient access to the very therapies that Congress sought to protect from the impact of the IRA’s policies, an absurd result that CMS can avoid by adopting a QSSD definition appropriately limited to FDA approval.

¹⁰ IRA § 1192(e)(3)(A).

¹¹ Initial Memorandum Section 30.1.1.

II. CMS IS IMPOSING AN ARBITRARY AND IMPROPER STANDARD WHEN DETERMINING WHETHER A GENERIC OR BIOSIMILAR IS MARKETED.

The IRA's statutory scheme focuses on drugs that have been on the market without generic or biosimilar competition. Congress intended that only those drugs that are truly "single source" may be selected for negotiation. The IRA accomplishes this by excluding from the QSSD definition a drug that is the listed drug for a generic that is marketed or a biologic that is the reference product for a biosimilar that is marketed.¹² Similarly, a selected drug exits that status if the Secretary determines that the selected drug has a generic or biosimilar that is marketed.¹³

CMS is frustrating Congressional intent by adopting an onerous, arbitrary, and ultimately unworkable definition of what it means for a generic or biosimilar to be "marketed." Further, CMS is basing its marketing determination solely on Part D prescription drug event ("PDE") data, which is not reflective of market reality and is therefore not a reliable indicator of when a drug is marketed.

A. CMS proposes an improperly narrow "marketing" determination that is subjective and arbitrary, opening the door to undisciplined and inconsistent agency determinations.

In the Initial Memorandum, CMS states that when determining whether a generic or biosimilar is being "marketed," it intends to analyze whether "robust and meaningful competition exists in the market," but does not define that standard further.¹⁴ Requiring "robust and meaningful competition" is vague and cannot be consistently applied across different products. Without consistent and transparent standards, it will be impossible for pharmaceutical manufacturers to accurately assess how the forced negotiation and capped price provision may apply to their products. A vague standard also will result in CMS making arbitrary determinations, creating an uneven playing field and unfairly favoring some drugs to the detriment of others.

CMS also states that it will consider a generic or biosimilar to be marketed when the PDE data reveal that the generic/biosimilar manufacturer has engaged in "bona fide marketing."¹⁵ The Initial Memorandum again does not clarify what "bona fide marketing" means. In the absence of a clear standard, the agency appears to be in a position where it will unilaterally determine when it deems a generic or biosimilar to be marketed.

CMS should clearly define the standard it will apply when making the "marketed" definition. The starting point for that definition should be the plain English meaning of the word "to market." Merriam Webster defines this as "to expose for sale in a market; sell," and defines "on the market" as "available for purchase."¹⁶ Fanciful terms like "robust and meaningful competition" and "bona fide marketing" have no basis in the IRA and serve only to arrogate to

¹² IRA § 1192(e)(1).

¹³ IRA 1192(c)(1).

¹⁴ Initial Memorandum Section 90.4.

¹⁵ Initial Memorandum Section 70.

¹⁶ *Marketed*, Merriam-Webster Dictionary (11th ed. 2003).

CMS the power to force drugs into the negotiation process by ignoring the existence of a generic or biosimilar—a power Congress never delegated to CMS or intended CMS to have.

B. The Initial Memorandum adopts inconsistent and contradictory definitions of “marketed.”

The Initial Memorandum proposes multiple, contradictory definitions of “marketed.” Appendix C of the Initial Memorandum sets forth information that CMS plans to collect from manufacturers during the negotiation process, and states that the term marketing “is defined as the introduction or delivery for introduction into interstate commerce of a drug product.” CMS should apply this definition, which is in line with the plain English meaning of “marketing,” throughout the Initial Memorandum, including when applying the exclusion from the QSSD definition. It is puzzling that the agency would define the same term in contradictory ways *in the same guidance document*—particularly when the IRA itself provides no basis for conflicting or even differing interpretations.

A marketing definition focused on “bona fide marketing” and “robust and meaningful competition” is also at odds with how CMS has defined marketing in other contexts. For example, in the Part D inflation rebate guidance¹⁷—which also implements the IRA—CMS proposes identifying the “first marketed” date of a drug as the “market date that the manufacturer is required to report” pursuant to the Medicaid Drug Rebate Program. For purposes of that program, CMS has defined “marketed” to mean “that a covered outpatient drug is available for sale by a manufacturer in the states.”¹⁸ Finally, for Medicare Part B purposes, CMS requires manufacturers to report a data field titled “Date of first sale.”¹⁹ Not surprisingly, that field is not further defined.

CMS has been able over the years to develop cogent “marketed” definitions and has even done so in Appendix C to the Initial Memorandum. In keeping with a plain English approach to statutory interpretation, CMS should adopt a clear standard for purposes of the QSSD exclusion, consistent with Appendix C. The agency should be even-handed in its application of the law and not adopt divergent definitions for the same concept in what can easily be perceived as an effort to expand its power under the IRA.

¹⁷ CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Sections 1860D-14B of Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (Mar. 15, 2023), available at <https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf>.

¹⁸ Medicaid Program; Announcement of Medicaid Drug Rebate Program National Rebate Agreement, 83 FR 12770, at 12772, available at <https://www.govinfo.gov/content/pkg/FR-2018-03-23/pdf/2018-05947.pdf>.

¹⁹ CMS, Medicare Part B Drug Average Sales Price (ASP) User Manual (Version 2.0, 2019) available at <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/Downloads/Medicare-Part-B-ASP-Data-Collection-User-Guide.pdf>.

C. CMS construes the meaning of “marketed” too narrowly by relying on PDE data to make its determination that a generic or biosimilar has been marketed.

CMS proposes to rely on PDE data for its determination that a generic or biosimilar is marketed and for subsequently monitoring whether the generic or biosimilar “is regularly and consistently available for purchase through the pharmaceutical supply chain, and whether it is available for purchase by community retail pharmacies in sufficient quantities from their wholesale suppliers.”²⁰ Exclusive reliance on PDE is inappropriate, and has no basis in the statute, as the IRA is concerned with whether the QSSD is “single source,” which is not the case when a generic or biosimilar is being marketed generally—regardless whether the generic or biosimilar enjoys widespread adoption by Part D.

Further, PDE data is unlikely to provide answers to the very inquiries that CMS proposes to undertake. A generic or biosimilar may well be “regularly and consistently available for purchase,” including by “community retail pharmacies,” but nevertheless such a drug may have little Part D utilization, such as because the generic manufacturer elected not to contract with Part D plans or had logistical issues achieving the necessary formulary positions. CMS’s proposed reliance on PDE data is also concerning because it is unclear which data fields CMS will elect to focus on. The term PDE data is broad and the data can be filtered to create summary extracts that would obscure whether a generic or biosimilar is present. There are other data sources CMS has access to that would allow the agency to understand the level of distribution of a drug, such as the National Average Drug Acquisition Cost (“NADAC”) data. Basing the “marketed” determination solely on Part D data is not reflective of market reality and therefore not a reliable indicator of when a drug is marketed.

A generic or biosimilar could also be available for sale, i.e., marketed, with little sales data because consumers or providers prefer the brand version for a variety of reasons. It would be inconsistent with the letter and spirit of the IRA to treat a drug as single source and refrain from excluding it from the QSSD definition or removing it from the selected drug list simply because sales data of a generic or biosimilar do not rise to a certain level in a certain market segment, both arbitrarily chosen and determined by CMS. In keeping with the plain English meaning of “to market,” CMS should determine whether a generic or biosimilar is “marketed” on the basis of whether a sale of the generic or biosimilar has occurred.

D. CMS appears to require 12 months of generic or biosimilar data prior to making a determination that it has been marketed.

The IRA provides that a selected drug will remain selected until “the first year that begins at least 9 months after the date on which the Secretary determines at least one” generic or biosimilar is approved and marketed.²¹ Therefore the timing of the determination is significant – a determination after March 31 of a given year will see the selected drug remain in that status for

²⁰ Initial Memorandum Section 90.4.

²¹ IRA § 1192(c)(1).

the entire following year, while a determination on or before March 31 would see the selected drug exit that status the following January.

In the Initial Memorandum, CMS proposes to determine whether a generic or biosimilar has been marketed each month, starting with October 2023.²² United Therapeutics agrees with a monthly determination, as this approach avoids the unfair impact inherent in the IRA’s 9-month holding period. However, CMS also proposes to base its marketed determination on PDE data from “the most recent 12-month period available to determine if the manufacturer of the generic drug or biosimilar biological product has engaged in bona fide marketing.”²³ According to the Initial Memorandum, for IPAY 2026, CMS intends to review PDE data for a given generic drug or biosimilar during the 12-month period beginning August 15, 2023 and ending August 15, 2023.²⁴

It is unclear if CMS intends to review data from within a 12-month period for its determination, or if CMS will require a complete 12 months’ worth of data before making the determination. Importantly, the IRA does not contemplate any period of review—likely because Congress expected CMS to ascribe a plain English meaning to “marketed,” where marketing occurs when the generic or biosimilar experiences a sale, not requiring a specific lookback period. CMS should clarify that it will not wait with making a marketed determination until 12 months of data is available. The alternative would impermissibly limit under what circumstances a generic or biosimilar is deemed to be marketed.

CMS also should institute a formal pathway for manufacturers to supply information about the marketing of a generic or biosimilar. Given the importance of the timing of the “marketed” determination, stakeholders should have the opportunity to supply essential information to CMS, and CMS should make assurances in any final guidance that the agency will review and consider the submission.

E. CMS proposes to engage in “monitoring” of whether a generic or biosimilar is “marketed,” with uncertain implications.

CMS indicates that even after making a determination that a generic or biosimilar is marketed, the agency will “monitor the manufacturers of generics or biosimilar biological products to ensure they are engaging in bona fide marketing of the generic or biosimilar biological product.”²⁵ The IRA contemplates no such monitoring. Furthermore, CMS does not indicate what the agency proposes to do on the basis of the results of such monitoring. The lack of clarity opens the door to troubling possibilities, such as whether CMS would revise a marketed determination as a result of such monitoring. The lack of clarity is itself an indication that CMS may be embarking on a pathway of arbitrary determinations. Given the significance of the marketing determination to a drug’s QSSD or selected drug status, CMS should make its intentions glaringly obvious rather than keeping stakeholders guessing as to the agency’s

²² Initial Memorandum Section 70.

²³ Initial Memorandum Section 70.

²⁴ Initial Memorandum Section 30.1.

²⁵ Initial Memorandum Section 30.1.

policy—and in keeping with the framework established by the IRA, CMS should abandon its poorly defined notion of monitoring the status of generics and biosimilars following a “marketed” determination.

III. CMS CORRECTLY PROPOSES THAT THE PRESENCE OF A SINGLE GENERIC OR BIOSIMILAR REMOVES THE DRUG FROM NEGOTIATION.

As noted above, the IRA focuses on single source drugs, which means that the reference or listed drug should not be considered to be single source if a generic or biosimilar is marketed. CMS proposes that the presence of a single generic or biosimilar removes the entire drug from QSSD status, and forms the basis for the entire QSSD exiting selected drug status. That is the correct interpretation, in keeping with the IRA statutory text, as well as Congressional intent. Further, CMS is appropriately applying the same legal standards in both instances—with respect to the exclusion from the QSSD definition, as well as with respect to a drug existing selected drug status.

United Therapeutics welcomes CMS’s proposal. However, given the significance of the QSSD definition and the related exclusion, it will be essential for the pharmaceutical industry to be able to rely on the applicable legal standards. For that reason, any final guidance should make clear that CMS commits to retaining this approach beyond 2026 and for subsequent IPAYs, including 2028 and beyond.

IV. CMS SHOULD NOTIFY THE MANUFACTURERS OF THE 50 NEGOTIATION-ELIGIBLE DRUGS.

United Therapeutics agrees with CMS’s approach to identify the 50 negotiation-eligible drugs solely based on a ranking of expenditures. We urge CMS to commit in any final guidance to retaining this approach beyond 2026 and for subsequent IPAYs, including with respect to Part B drugs, beginning in 2028.

In the interest of transparency, CMS should notify the manufacturers of negotiation-eligible drugs as soon as CMS has identified these drugs, so that the affected manufacturers can prepare in advance for possible selection of their drugs for negotiation. The disclosure should indicate where a particular drug is ranked among the 50 negotiation eligible drugs, thereby providing additional insight to manufacturers as to the likelihood of being selected for negotiation in subsequent IPAYs. This advance notice would also allow the manufacturer more time to prepare the necessary information for CMS and would give manufacturers the opportunity to notify CMS if a drug is included among the negotiation eligible drugs in error. Transparency would thus benefit not only the manufacturer, but also CMS, as the agency would be able to evaluate the manufacturer concerns ahead of making the selection and could avoid costly mistakes.

In the case of biologics, this type of notification would also enable the manufacturer of the QSSD to inform the manufacturer of a potential biosimilar of the likelihood that the biologic would be selected for negotiation, which would enable the biosimilar manufacturer to consider whether to avail itself of the biosimilar delay process. Without this level of transparency, it is unclear how biosimilar manufacturers would determine whether and when to do so.

V. CMS SHOULD REMOVE UNNECESSARY OBSTACLES WHEN ESTABLISHING “HIGH LIKELIHOOD” OF IMMINENT LICENSURE OF A BIOSIMILAR.

The IRA provides that the sponsor of a biosimilar can apply to CMS to delay inclusion of the reference product as a selected drug for up to two years if there is a “high likelihood” that the biosimilar will be licensed and marketed within the specified period. The Initial Memorandum establishes certain unnecessary obstacles that the manufacturer of a biosimilar must satisfy to avail itself of this process.

A. CMS should not dismiss applications where there is active patent litigation between the reference product manufacturer and the biosimilar manufacturer.

CMS proposes to reject an application from the biosimilar manufacturer if there is active litigation between the biosimilar and reference product manufacturers regarding the reference product’s patents.²⁶ Such an exclusion is overly broad, particular as patent-related litigation is exceedingly common in instances where release of a biosimilar is imminent. It is accurate, as CMS states, that patent litigation is “highly unpredictable,” but outright rejection of applications on that basis is not consistent with the IRA and would be tantamount to invalidating the entire mechanism. CMS instead should consider the application on its merits and should evaluate the existence of patent litigation as just one factor in its evaluation.

B. CMS should focus its determination of high likelihood on the status of the biosimilar’s BLA application.

CMS proposes that the application must clearly demonstrate that the biosimilar manufacturer “will be operationally ready” to timely market the biosimilar. CMS suggests it will consider the manufacturer’s progress “against the actions, activities, and milestones that are typical of the normal course of business leading up to the marketing of a drug.” Unfortunately, it is unlikely that CMS possesses sufficient expertise to understand what is “typical” in the lead-up to launching a drug, creating the potential for flawed determinations and arbitrary actions by the agency. Further, launch preparation and timing will vary significantly from product to product, based on unique aspects of each therapy and each manufacturer’s distribution model. For that reason, CMS should focus its high likelihood determination on objectively ascertainable facts, such as the status of the BLA application for the biosimilar. When evaluating subjective factors, such as operational readiness, CMS should give deference to the assertions made by the biosimilar manufacturer in its application.

C. CMS is too prescriptive as to the types of documents that may be submitted to support a finding of “high likelihood.”

The Initial Memorandum proposes factors CMS will apply to determine whether a “high likelihood” exists that a biosimilar will be licensed and marketed. CMS specifically requires disclosures about capital investments (or comparable documents for privately held companies),

²⁶ Initial Memorandum Section 30.3.1.2.

revenue expectations and manufacturing schedules. While these are examples of documents that can be expected to be available to biosimilar manufacturers in the normal course of business, CMS is too restrictive when it limits applicants to these particular types of documents. Circumstances are likely to vary significantly by manufacturer. CMS should instead be less prescriptive with respect to the types of information that the biosimilar manufacturer may provide, and CMS should make this process as flexible and principle-based as possible.

D. CMS should notify reference manufacturers of both successful and unsuccessful applications.

CMS proposes to notify the manufacturer of the reference biologic of a successful application for delay from a biosimilar manufacturer.²⁷ United Therapeutics urges CMS to also provide notification in the case of unsuccessful applications to provide additional transparency to all stakeholders. In particular, manufacturers that are public companies and therefore subject to periodic reporting obligations may need to consider this information for their disclosures.

VI. THE PROPOSED DEFINITION OF “MANUFACTURER” IS OVERLY BROAD AND IMPRECISE.

In the Initial Memorandum, CMS broadens the definition of manufacturer to include so-called “secondary manufacturers,” which CMS defines as an entity that “markets the selected drug pursuant to an agreement with the Primary Manufacturer as a ‘Secondary Manufacturer.’”²⁸

The IRA defines manufacturer by reference to section 1847A(c)(6)(A) of the Social Security Act, which in turn, cross-references section 1927(k)(5). CMS does not clearly explain in the Initial Memorandum how it seeks to implement these very broad statutory definitions, which generally focus on entities engaged in the production or packaging of drugs (as quoted below). The agency uses phrases such as “of the selected drug” when referring to the manufacturer, which is imprecise and not helpful when applying the broad statutory definition in a particular context. In Medicaid regulations, CMS has clarified the 1927(k)(5) manufacturer definition to refer to “any entity that holds the NDC for a covered outpatient drug or biological.”²⁹ CMS should provide similar clarity here using the same approach.

The secondary manufacturer definition is troubling because of its similar lack of precision. The Social Security Act definition of manufacturer at section 1927(k)(5) refers to “any entity which is engaged in—(A) the production, preparation, propagation, compounding, conversion, or processing of prescription drug products, either directly or indirectly by extraction from substances of natural origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis, or (B) in the packaging, repackaging, labeling, relabeling, or distribution of prescription drug products.”³⁰ An entity could meet this definition by virtue of manufacturing a drug, but not the primary manufacturer’s drug, and could then

²⁷ Initial Memorandum Section 30.3.1.4.

²⁸ Initial Memorandum Section 40.

²⁹ 42 CFR 447.502 “Manufacturer.”

³⁰ Social Security Act § 1927(k)(5).

contract with the “primary” manufacturer to market the primary manufacturer’s drug. In this scenario, this entity, although not involved in the manufacture of the primary manufacturer’s drug at all, could be deemed a secondary manufacturer under the definition proposed by CMS. The Initial Memorandum must clarify the scope of the secondary manufacturer definition to make it appropriately precise.

CMS acknowledges this issue in Section 90.2 of the Initial Memorandum, stating that “it is possible for an entity that meets the statutory definition of a manufacturer, but that is not the Primary Manufacturer or a Secondary Manufacturer, to market one or more drug or biological products pursuant to one or more NDA(s) or BLA(s) included in the selected drug.”³¹ The primary manufacturer should have no obligations regarding the conduct of such entities, including with respect to whether such entities are making the MFP available to MFP-eligible individuals.

VII. MANUFACTURER CONFIDENTIAL INFORMATION MUST BE AFFORDED GREATER PROTECTION, AND MANUFACTURERS MUST BE ALLOWED TO DISCLOSE INFORMATION REGARDING THE NEGOTIATION PROCESS.

The Initial Memorandum indicates that for IPAY 2026, CMS intends to treat as proprietary only certain data elements submitted by a primary manufacturer.³² The scope of information that is by definition treated as confidential should be expanded. CMS also seeks to restrict the information about the negotiation process that the manufacturer may disclose or even retain. Such restrictions are not appropriate and must not be included in any final guidance.

A. CMS must afford greater protections to manufacturer confidential information.

The IRA requires that manufacturers make extraordinary disclosures to CMS, including information necessary for CMS to negotiate with the manufacturer. CMS should defer to the manufacturer’s designation of these disclosures as proprietary and confidential, rather than, as proposed, treating only limited categories of information as confidential. This approach should apply to information initially provided by the manufacturer, as well as any information provided by the manufacturer during the negotiation process. CMS is a government agency and as such should rely on market participants that possess the necessary sophisticated understanding of commercial reality and are in a better position to assess whether information is proprietary and confidential or not. Therefore it is appropriate for CMS to defer to manufacturers regarding these determinations. United Therapeutics agrees with the Initial Memorandum that, in accordance with the IRA, any proprietary information may be used only for “purposes of carrying out the Negotiation Program.”³³

³¹ Initial Memorandum Section 90.2.

³² Initial Memorandum Section 40.2.1. For IPAY 2026, CMS proposes to treat as proprietary the following: All non-FAMP information, commercial or financial information that cannot be found publicly, research & development costs and recoupment, unit costs of production and distribution, pending patent applications, market data and revenue and sales volume data.

³³ *Id.*

CMS should limit its disclosure when publishing the MFP explanation to information already available in the manufacturer's public company or similar filings—that is, already public information. The Initial Memorandum indicates that CMS intends to make “high-level comments about the data submitted to CMS, without sharing any proprietary information reported to CMS,” such as “the manufacturer has recouped its research and development costs.”³⁴ To avoid any inadvertent disclosure, prior to publication of this public explanation, CMS should give the affected manufacturer an opportunity to review the publication and to designate any information therein that is confidential and proprietary.

B. CMS should allow manufacturers to retain and disclose information regarding their negotiation with CMS.

The Initial Memorandum proposes to require that manufacturers may “not ...disclose to the public any information in the initial offer or any subsequent offer by CMS, the ceiling price contained in any offer, or any information contained in any concise justification provided with an offer.”³⁵ This is wholly inappropriate. Manufacturers should be allowed in their discretion to disclose to the public information about their negotiation with CMS to provide transparency, particularly if a manufacturer disagrees with CMS's characterization of the negotiation in its public explanation for determining the MFP. Such an unreasonable restriction may also contradict other legal disclosure obligations the manufacturer may be subject to.

Further, manufacturers should not be required to agree “that all information the Primary Manufacturer receives during the negotiation period from CMS shall be destroyed within 30 days of a determination by CMS that the drug or biologic no longer qualifies as a selected drug, except as may be required by applicable state or federal law.”³⁶ Manufacturers should be allowed to retain records of the negotiation process. It is troubling that CMS would seek to impose such an unreasonable obligation, which would deprive the manufacturer of recourse if the manufacturer were to subsequently become subject to challenge regarding how it conducted the negotiation.

CMS lacks statutory authority to require that all manufacturer agreements incorporate these non-disclosure and information destruction provisions. While the IRA directs the Secretary to enter into manufacturer agreements under which “the manufacturer complies with requirements determined by the Secretary to be necessary for purposes of administering the program and monitoring compliance with the program,”³⁷ CMS's wholly inappropriate mandatory non-disclosure and information destruction provisions are not necessary to administer or monitor compliance with the negotiation program.

³⁴ Initial Memorandum Section 40.2.1.

³⁵ Initial Memorandum Section 40.2.2.

³⁶ *Id.*

³⁷ IRA § 1193(a)(5).

VIII. THE STATUTORY CEILING PRICE, NOT THE PRICE OF ALTERNATIVE TREATMENTS, SHOULD BE THE STARTING POINT FOR CMS'S INITIAL OFFER DURING NEGOTIATION.

The IRA sets out that the MFP developed during the negotiation process may not exceed the statutory ceiling price, the only specific price defined in the IRA. The statute also provides certain negotiation factors that CMS must consider when conducting the negotiation process.³⁸ The negotiation begins with an initial offer proposed by CMS to the manufacturer. In the Initial Memorandum, CMS proposes to develop that initial offer by primarily relying on just one of these factors, namely the price for alternative treatments in the therapeutic space. Taking a page from the real estate playbook, CMS appears to be searching for “comparables” to the selected drug, intending to then base the initial offer on the price for such comparable therapies. CMS proposes to then use the other negotiation factors merely to adjust that initial offer. While appearing as a convenient shortcut for the agency, this approach is fundamentally flawed. Instead, the statutory ceiling price should be the starting point for CMS's initial offer, which CMS can then adjust, if appropriate, by reference to the negotiation factors—not just by reference to a single negotiation factor.

By definition, the drugs subject to negotiation have been marketed for longer periods without a generic or biosimilar and represent the highest amounts of Medicare spending. By their very nature, such drugs are unlikely to have therapeutic alternatives that can provide similar patient benefits; otherwise, the market (without government intervention) would already have shifted toward such alternatives.

This weakness is highlighted by CMS's overreach: In order to make this approach feasible, CMS is going so far as proposing to include off-label uses of the selected drug. CMS proposes to consider “off-label use when identifying indications [of the selected drug] if such use is included in nationally recognized, evidence-based guidelines and recognized by CMS-approved Part D compendia.”³⁹ In other words, CMS might prepare an initial offer on the basis of the prices for therapeutic alternatives to an *off-label use* of the selected drug. This is an unsound approach that fails to assign any value to the selected drug's FDA approval, disregarding the costs and risks that obtaining such approval entailed. Off-label indications should not be taken into account for purposes of obtaining therapeutic alternative prices, and frankly should have no place at all in the federal regulatory scheme.

CMS also indicates that it will rely on ASP figures when identifying the prices for therapeutic alternatives. Only a Part B drug (generally, a physician-administered drug) would have an ASP figure available, but only Part D drugs (generally, self-administered) are subject to negotiation in IPAY 2026. These different methods of administration indicate that Part D and B drugs, even if in the same therapeutic space, are not at all comparable. For example, Part B drugs are often infused, and manufacturers of infusion drugs have, where possible, invested considerable resources to create and gain approval for presentations that can be administered subcutaneously and are thus self-administered. CMS's proposal to include Part B drugs when identifying prices

³⁸ IRA Section 1194(3).

³⁹ Initial Memorandum Section 60.3.1.

of therapeutic alternatives for IPAY 2026 is therefore misguided and fails to account for the greater patient benefits often associated with self-administered (i.e., Part D) drugs.

Where genuine (i.e., not off-label) alternative therapies with prices below the statutory cap are not available, CMS proposes to rely on Federal Supply Schedule or “Big Four” pricing to prepare its initial offer.⁴⁰ These prices are based on the Non-Federal Average Manufacturer Price (“Non-FAMP”) metric, resulting in a circular logic: The MFP is capped by reference to Non-FAMP, and CMS is proposing to commence the negotiation with an offer that is also based on Non-FAMP. The appropriate approach in this scenario is readily at hand: Where no therapeutic alternatives are available, or the therapeutic alternatives are priced higher than the IRA capped price, CMS should offer the IRA capped price as its initial offer, which would likely conclude the negotiation.

Thus any final guidance should provide that the starting point for CMS to prepare the initial offer should be the statutorily capped price, rather than an arbitrary reference price for purported therapeutic alternatives. CMS should operate under the presumption that the MFP should be lower than the statutory cap only where application of the IRA’s negotiation factors supports such a further reduced price. This is appropriate, because the basis for the statutory cap—Part D expenditure or Non-FAMP, which generally reflects prices to wholesalers net of discounts—reflects the patient benefits provided by the selected drug. The statutory ceiling price is the only price that is specifically defined in the IRA. CMS should assign it the same significance that Congress has.

IX. IN REVIEWING THERAPEUTIC ALTERNATIVES, CMS SHOULD NOT RELY ONLY OR PRIMARILY ON LITERATURE ADDRESSING THE MEDICARE POPULATION.

As noted, one of the IRA’s negotiation factors considers therapeutic alternatives to the selected drug.⁴¹ The statute makes clear that when reviewing therapeutic alternatives, CMS may not rely on literature that treats as less valuable extending the life of an elderly, disabled, or terminally ill person. United Therapeutics wholeheartedly agrees with this policy. However, the Initial Memorandum oddly misconstrues this requirement. It provides that CMS intends to consider “research and real-world evidence relating to Medicare populations, including individuals with qualifying disabilities, patients with end-stage renal disease (ESRD), and Medicare-aged populations, *as particularly important*.”⁴²

CMS should not rely only or primarily on data that addresses the Medicare population or which treats extending the life of an elderly person as more valuable than that of younger, non-disabled, or non-terminally ill persons, as neither the statute nor prudent policy support such an interpretation. The ultimate MFP will only apply to the Medicare program, but the MFP (and its justification) will be publicly available, and private payors and other stakeholders outside of

⁴⁰ Initial Memorandum Section 60.3.2.

⁴¹ Initial Memorandum Section 50.2.

⁴² *Id.* (emphasis added).

Medicare will rely on and utilize the MFP to conduct their own negotiations with the manufacturer.

This puts CMS in a unique position to impact the availability of drugs and therapeutic alternatives to patients outside of Medicare. CMS must give careful consideration to the ramifications of its negotiation position. One way it can exercise care is by giving substantial weight to literature that addresses the drug and its therapeutic alternatives in populations other than the elderly, disabled, or terminally ill. The QSSD determination focuses on general attributes of the drug, such as years since approval. There is no basis in the statute to deviate from this general approach in this instance by focusing the negotiation on particular patient populations.

X. WHEN APPLYING THE NEGOTIATION FACTORS, CMS SHOULD CONSIDER INDIRECT RESEARCH AND DEVELOPMENT COSTS, AND SHOULD DISREGARD THE LENGTH OF PATENT PROTECTION AND EXCLUSIVITY.

One of the IRA’s negotiation factors refers to research and development costs for the selected drug, and whether the manufacturer has recouped these costs. CMS appears to treat recoupment of research and development costs as specific to the particular selected drug, but the agency has not considered that for every product that a manufacturer brings to market, a large number of products end in failure during the clinical and pre-clinical trial phases. CMS should allow manufacturers to report, and CMS should consider, the research and development costs of the many failed drug candidates when assessing the research and development costs for the selected drug, and the degree to which these costs have been recouped.

Furthermore, costs associated with an approved drug may actually relate to the clinical and other data generated for an earlier drug; that is, the costs associated with a given drug are not neatly delineated. This means that manufacturers may need to provide CMS with costs associated with the earlier drug because these costs are indirect costs that affect the price of the successfully-marketed drug. All the while, the sales associated with the earlier drug should not be counted toward the “recoupment” of costs of the subsequent drug. In light of these complexities, CMS must be cognizant of the difficulties inherent in allocating costs to specific products, especially if a manufacturer has a large product portfolio. Any final guidance therefore must specifically allow manufacturers to report these additional, indirect costs that are associated with the selected drug.

The Initial Memorandum indicates that CMS “intends to consider the length of the available patents and exclusivities before the selected drug may no longer be single source.”⁴³ For example, “if the selected drug has patents and exclusivities that will last for a number of years, CMS may consider adjusting the preliminary price downward.”⁴⁴ There are a number of grave issues with this approach, first and foremost that CMS is arbitrarily creating a negotiation factor not contemplated by the IRA. The statute is very clear when describing the negotiation factors, making clear that Congress intended to establish the parameters for negotiation. Nothing in the

⁴³ Initial Memorandum Section 60.3.4.

⁴⁴ *Id.*

IRA supports considering patent protection and exclusivity during the negotiation in the manner proposed by CMS.

Further, CMS's proposal runs counter to basic tenets of FDA legal standards and the U.S. patent system. Manufacturers should be rewarded, not penalized with a downward adjustment of the preliminary price, for innovating and investing in the collection of clinical data justifying an extension of regulatory exclusivity. CMS's interpretation limits manufacturers' ability to recoup expenses for their investments that benefit patients, such as conducting a pediatric clinical trial that may result in obtaining pediatric exclusivity. The patent system is based on the notion that the reward for innovation is patent protection and exclusivity, and CMS is turning this long-standing framework on its head.

XI. CMS SHOULD MORE CLOSELY ALIGN THE NEGOTIATION PROCESS WITH COMMERCIAL NEGOTIATIONS.

In some respects, the Initial Memorandum seeks to characterize the IRA negotiation process as akin to a commercial negotiation between equal market participants. In fact the negotiation is a forced process with a forgone conclusion, namely that the price is capped—but CMS nevertheless has leeway under the IRA to align the process with commercial negotiations, and to forego some of the authoritarian elements present in the Initial Memorandum.

A. CMS should not limit the number of negotiation meetings.

CMS proposes that there will be up to a total of three negotiation meetings between CMS and the manufacturer. United Therapeutics agrees that the negotiation process should not be limited to written exchanges, but disagrees with limiting the meetings to a total of three. Given the significance of the outcome of this process, there should be flexibility to allow for more than three meetings. It is also unclear whether a phone call to clarify specific points or some other interaction qualifies as a "meeting" and would occupy one of the three slots. As in any other negotiation, a party can reject an invitation to a meeting. Therefore the guidance should provide for a minimum number of meetings, but should not impose a limitation as to the total number of meetings. CMS leadership has indicated the agency's intention to simulate a genuine negotiation, as would occur in the commercial market. Any final guidance should not limit the number of meetings.

B. If both CMS and the manufacturer engage in a bona fide negotiation that yields no agreement, the resulting MFP should be the statutory ceiling price.

The IRA provides a timeframe for the negotiation process, including when that process ends. But the IRA does not indicate how to proceed if the negotiation period ends without an agreement as to the MFP. The Initial Memorandum similarly does not address this circumstance, other than to state that the manufacturer is required to respond in writing to the final CMS offer, and that "CMS will notify the Primary Manufacturer of any failure to meet the deadline and the possible consequences thereof if no MFP agreement by July 31, 2024."⁴⁵ The Initial Memorandum also provides that if no MFP is agreed to, CMS will not publish an MFP or an

⁴⁵ Initial Memorandum Section 60.4.4.

explanation, and will indicate on its website only the absence of agreement. Finally, the Initial Memorandum contemplates that the manufacturer might agree to an MFP after the negotiation period ends.

If the manufacturer has satisfied its obligation to participate in the negotiation process as outlined in the IRA and in the manufacturer agreement, and no MFP is agreed to at the end of the negotiation period, the statutory ceiling price should be the MFP. This result is in keeping with the IRA statutory intent of achieving a capped price and coupling the price cap with a negotiation process. If both parties genuinely followed the statutory requirements related to the process, the default result should be the statutorily capped price, and the manufacturer should not be exposed to civil monetary penalties or other enforcement mechanisms. Any other result would reveal that CMS has overstepped its authority by mandating, rather than negotiating, a price—by essentially treating its final offer as one the manufacturer is required to agree to. Congress mandated a price, as it has done via the price cap, but CMS can merely negotiate a price. If a genuine negotiation process that complies with the IRA fails to yield agreement, the default MFP should be the capped price mandated by Congress which, as noted, is the only price specifically defined in the IRA.

XII. THE OVERLY BROAD QSSD DEFINITION MAKES COMPLEX MFP AND CEILING PRICE CALCULATIONS NECESSARY, WHICH CANNOT ACCURATELY REFLECT DRUG USE REALITIES.

The Initial Memorandum describes how CMS will establish a single proposed MFP for negotiation purposes, and how CMS will determine the statutory ceiling price for the selected drug. This process would be comparatively straightforward if the QSSD definition were limited to a specific FDA approval. However, given the expansive QSSD definition that CMS is proposing—encompassing all of a manufacturer’s FDA approvals, dosage forms, and strengths that share the same active moiety or active ingredient—the need to arrive at a single MFP and a single statutory ceiling price makes it necessary to perform complex calculations. The calculations CMS proposes have no basis in the statute and were not contemplated by Congress. But more detrimentally, they do not properly reflect the nature of many drugs or how they are administered over time. Furthermore, CMS has not provided detail on how it will perform important steps in the calculations, as well as necessary unit conversions. CMS should abandon its overly broad QSSD definition and instead define QSSD to correspond to a specific FDA approval, which would make these complex calculations unnecessary. Indeed, operationalizing the statutory MFP language in conformity to the IRA is only possible if CMS revises its QSSD definition to refer to FDA approval.

A. The single MFP that CMS proposes to calculate across FDA approvals, dosage forms, and strengths (including different unit types) does not reflect the nature or administration of drugs.

At each step of the negotiation process, CMS proposes to offer a single MFP which it will then apply to the drug’s multiple dosage forms, strengths, and unit types.⁴⁶ CMS will base the single price on the average cost of the selected drug per 30-day equivalent supply—rather than per

⁴⁶ Initial Memorandum Section 60.1.

unit—averaged across dosage forms and strengths. CMS believes this approach is justified because it will allow for a more direct comparison with therapeutic alternatives.

The Initial Memorandum accurately states that the IRA requires that a single price be negotiated for each selected drug. But the overly broad QSSD definition, which cuts across dosage forms, strengths, unit types, and FDA approvals, forces CMS to now also stretch the notion of what a “price” can be. The proposed approach of focusing on a cost per 30-day “equivalent” supply, weighted across dosage forms and strengths, is a statistical ploy that will fail to accurately reflect the costs associated with the various presentations encompassed by the QSSD definition.

For instance, the 30-day supply is a proper understanding of drug usage for traditional drugs—take one tablet per day. This understanding of drug therapies would have been adequate when the Medicaid Drug Rebate Program was enacted in 1991, but it is no longer sufficient in 2023. Pharmaceutical innovation has resulted in complex therapies, with dosage requirements varying widely across specific patients, and varying over time, not to mention single-use curative therapies.

For example, Orenitram® requires a flexible titration schedule, and may have continued titration and varying dosage throughout a specific patient’s therapy. Ultimately, the cost of therapy for one patient may be multiples of the cost for another patient during the same period of time. It is simply not feasible to derive a 30-day “equivalent” cost for these types of complex therapies.

B. CMS has not provided important details of how it proposes to calculate the IRA ceiling price, including unit conversions.

The IRA establishes a price cap on the basis of the greater of historic Medicare spend or average Non-FAMP. Contrary to what the IRA provides or what Congress intended, the overly broad QSSD definition makes it necessary to calculate the price cap across different dosage forms, strengths, and unit types. When determining the historic spend or average Non-FAMP figures for purposes of determining the ceiling price, CMS proposes to again utilize a per 30-day “equivalent” supply.

For historic spend, CMS also is engaging in various conversion calculations to move from data at the NDC-11 level to a single amount for the entire QSSD, across NDC-11s, dosage forms, and strengths. CMS fails to provide important details as to how this calculation will be performed. Similarly, for Non-FAMP, CMS proposes to convert Non-FAMP units to historic spend (PDE) units so as to allow the historic spend and Non-FAMP numbers to be comparable. CMS does not provide any details as to how this unit conversion would be performed.

Any final guidance should align Non-FAMP determinations with long-standing Department of Veterans Affairs (“VA”) legal standards. Non-FAMP is a metric that the VA has collected from manufacturers since 1992, and the VA already has addressed various circumstances related to Non-FAMP reporting. For example, the VA permits restatements of Non-FAMP in various circumstances. CMS should provide an equivalent mechanism for Non-FAMP restatements. As is the case with price metrics reported to CMS, like Average Manufacturer Price, there can be anomalies in the Non-FAMP calculation. CMS should adopt the same override rules that the VA has provided in order to address such circumstances.

We are furthermore concerned about the accuracy of these calculations and transparency throughout the negotiation process. Given that CMS will only include a “concise justification”⁴⁷ for its offer and that CMS may not make an offer that exceeds the drug’s IRA ceiling price, manufacturers may not have the ability to review CMS’ calculations for arriving at the ceiling price as an initial matter. CMS should include in its concise justification a copy of its calculations to show precisely how it arrived at the purported ceiling price so that the manufacturer can take this information into account when formulating a counteroffer.

This Initial Memorandum and its complex MFP and ceiling price calculations are focused solely on Part D drugs, because only Part D drugs are subject to negotiation for IPAY 2026. However, Part B drugs will enter the process in IPAY 2028. CMS should have developed a pricing methodology for 2026 that can easily be adapted for Part B drugs as well, but CMS has not done so. As a result of the too broad QSSD definition, CMS is proposing an overly complex approach that, when applied to Part B drugs, will result in yet more complicated unit conversions, as there is even greater variety in Part B billing units.

XIII. THE OVERLY BROAD QSSD DEFINITION MAKES A COMPLEX CALCULATION NECESSARY TO DERIVE AN MFP AT THE PER UNIT LEVEL.

As described above, the overly broad QSSD definition makes complex calculations necessary to derive a single MFP that applies across dosage forms, strengths, and unit types. This then means that the final MFP resulting from the negotiation has to be converted yet again, this time to a per-unit price, so that it can be effectuated in the marketplace. Once again, CMS can eliminate these difficulties and complexities by adopting a QSSD definition in any final guidance that aligns with the IRA and statutory intent and defines a QSSD by reference to a single FDA approval.

The process CMS proposes for breaking the MFP down to a per-unit level, undoing the prior aggregation across dosage forms and strengths (i.e., across NDC-9s), refers to how the Wholesale Acquisition Cost (“WAC”) price for the QSSD differs between NDC-9s (and units). In other words, CMS proposes to use the QSSD’s WAC distribution across NDC-9s (and units) as the reference to then distribute the MFP across NDC-9s (and units) in the same proportion.

WAC is defined in the Medicare statute as “the manufacturer's list price for the drug or biological to wholesalers or direct purchasers in the United States, not including prompt pay or other discounts, rebates or reductions in price, for the most recent month for which the information is available, as reported in wholesale price guides or other publications of drug or biological pricing data.”⁴⁸ Because it does not reflect discounts, WAC is an imperfect measure of the actual price in the market. CMS should consider other price metrics it has available, such as NADAC data, in order to achieve an MFP price per unit that is more aligned with market reality.

⁴⁷ Initial Memorandum Section 60.4.1.

⁴⁸ Social Security Act § 1847A(c)(6)(B) (emphasis added).

Additionally, it is worth noting that WAC changes over time as manufacturers modify their prices. The Initial Memorandum proposes to use WAC for calendar year 2022,⁴⁹ but does not appear to account for WAC changes during that year. Any final guidance that utilizes WAC as the basis for the MFP price distribution across NDC-9s must consider WAC changes in the period.

XIV. CMS SHOULD CLARIFY THAT FOR IPAY 2026, THE MFP IS APPLICABLE ONLY TO PART D UTILIZATION.

Consistent with the IRA, the Initial Memorandum defines MFP-eligible individuals as Part D and Part B beneficiaries.⁵⁰ But the guidance fails to make clear that for 2026, the MFP is applicable only to Part D utilization, not Part B utilization. Any final guidance must make clear that the MFP for 2026 applies to Part B beneficiaries only when receiving a drug under Part D, and that the MFP does not apply when the beneficiary is administered a drug under Part B. This distinction is particularly important because CMS's overly broad QSSD definition results in Part D and B drugs being included as the same QSSD, a circumstance the IRA does not address, and Congress did not contemplate.⁵¹

XV. CMS SHOULD NOT REGULATE THE MECHANISM WHEREBY MANUFACTURERS MAKE THE MFP AVAILABLE TO ELIGIBLE INDIVIDUALS.

The IRA provides that the manufacturer “shall” provide the MFP to eligible individuals at the point of sale.⁵² Yet the Initial Memorandum proposes to require the manufacturer to “ensure” dispensing entities have access to the MFP, and to require submission to CMS of the manufacturer’s process for making the MFP available.⁵³ CMS then proposes to publish the process on its website. Further, in the Initial Memorandum, CMS requires that manufacturer may make the MFP available to pharmacies, by (1) ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP or (2) providing “retrospective reimbursement” for the difference between the dispensing entity’s acquisition cost and MFP.⁵⁴

Manufacturer obligations are sufficiently clear in the IRA, and it is patently unnecessary for CMS to attempt to regulate in detail how the MFP is to be effectuated. CMS may be becoming a market participant by virtue of the forced negotiation process, but the agency should not overstep its boundaries by seeking to regulate commercial arrangements between manufacturers and other participants in the supply chain, even if the manufacturer has become subject to drug price

⁴⁹ Initial Memorandum Section 60.5.

⁵⁰ Initial Memorandum Section 80.

⁵¹ Importantly, CMS cannot cure the problem we discuss above caused by the overly broad QSSD definition, namely that the Part B reimbursement rate for a Part B drug that is swept into the QSSD (and therefore selected drug) definition is equal to MFP plus 6 percent, not ASP plus 6 percent. This is a statutory requirement. IRA § 1198(b)(1)(A).

⁵² IRA § 1193(a)(3)(A).

⁵³ Initial Memorandum Sections 40.4 and 90.2.

⁵⁴ Initial Memorandum Section 40.4.

negotiations. As with other federal programs that require ceiling prices—such as the VA federal supply schedule pricing program—commercial actors are best equipped to develop the mechanics for making these prices appropriately available.

Finally, there is no reason why commercial arrangements that the manufacturer enters into to effectuate the MFP should be disclosed to CMS, let alone be published by CMS on its website. The IRA contemplates no such measures, and such requirements would again raise confidentiality concerns. In the absence of a mandate by Congress, CMS should allow free market participants to develop their own commercially viable approaches and not interfere in the pharmaceutical marketplace.

XVI. AFTER AN NDA OR BLA TRANSFER, CMS SHOULD NOT HOLD THE PRIOR NDA/BLA HOLDER RESPONSIBLE FOR MAKING THE MFP AVAILABLE.

The Initial Memorandum provides that the agreement to negotiate that manufacturers have to enter into “shall be effective, with respect to a selected drug, until such drug is no longer considered a selected drug.”⁵⁵ Like the overly broad QSSD definition, this scope exceeds the IRA and Congressional intent. CMS is proposing to disregard NDA/BLA transfers, with the original manufacturer remaining responsible for making the MFP available, unless the original manufacturer transfers that obligation to the new NDA/BLA holder.

Not only is this further CMS overreach, it is also internally inconsistent. CMS proposes to define QSSD in part by reference to the manufacturer holding the NDA or BLA. Nevertheless, in the context of transfers, CMS is proposing to disregard that ownership. Transfer of an NDA/BLA to a manufacturer that does not have a negotiation agreement with CMS in place must remove that NDA/BLA from the QSSD definition and selected drug status.

XVII. CMS SHOULD SPECIFY THAT WHERE THE MFP IS LOWER THAN THE 340B CEILING PRICE, ONLY 340B OR MFP ELIGIBLE INDIVIDUALS MAY RECEIVE THE MFP.

The IRA provides that the manufacturer is “required to provide access to the maximum fair price to [a 340B] covered entity with respect to maximum fair price eligible individuals who are eligible to be furnished, administered, or dispensed such selected drug at such entity at such [340B] ceiling price in a non-duplicated amount to the [340B] ceiling price if such maximum fair price is below the [340B] ceiling price for such selected drug.”⁵⁶ The Initial Memorandum fails to make clear that the manufacturer must provide the MFP to 340B covered entities only with respect to “maximum fair price eligible individuals” who are otherwise eligible to be dispensed 340B-priced drugs.

It is essential that CMS correctly implement the boundaries of MFP eligibility in any final guidance. This is fundamental to the proper realization of the IRA’s statutory scheme: The manufacturer is required to provide to a 340B covered entity the lower of either (1) the 340B ceiling price or (2) the MFP, but only “with respect to maximum fair price eligible individuals”

⁵⁵ IRA § 1193(b).

⁵⁶ IRA § 1193(d)(2).

who are eligible to receive the drug “at such entity at such [340B] ceiling price.” If the MFP is lower than the 340B ceiling price, the covered entity is entitled to the MFP only as to individuals eligible to receive 340B-priced drugs, i.e., patients of the covered entity. Any final guidance should provide a requirement that the 340B covered entity verify 340B patient eligibility to the manufacturer before requesting to purchase the selected drug at the MFP—that is what the IRA requires, and CMS must implement this requirement in any final guidance.

Further, while the statute is clear that the manufacturer is required to provide either the 340B ceiling price or the MFP, but not both, the Initial Memorandum obfuscates this requirement through the use of imprecise language. CMS should clearly reflect in any final guidance what the IRA provides, namely that duplicate discounts are illegal: A unit can either be subject to the 340B price or the MFP.

Given the long-standing duplicate discount issues involving the 340B program, CMS should provide a mechanism to guard against MFP/340B duplicate discounts. If the MFP is effectuated through a rebate, it is likely that duplicate discounts could arise, with the covered entity claiming the 340B price at time of purchase and later submitting for a rebate to also receive the MFP, much like covered entities do in the Medicaid context, in violation of statutory requirements. CMS can guard against such duplicate discounts right from the outset by requiring the use of claims modifiers to reliably identify 340B utilization.

In the same way that the MFP can be effectuated through a rebate, so too can the 340B ceiling price, an approach the Health Resources and Services Administration (“HRSA”) has adopted for AIDS Drug Assistance Program grantees. The implementation of the MFP through a rebate mechanism provides an opportunity to implement the 340B discount for all types of covered entities through a rebate as well. This would finally address long-standing problems with the 340B program, while also simplifying the implementation of the MFP. We encourage CMS to collaborate with HRSA in the coming months and issue joint guidance addressing implementation of the MFP and 340B price through a rebate.

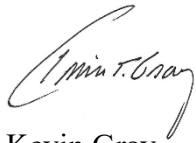
XVIII. CONCLUSION

The IRA imposes a European, government-controlled pricing model onto the U.S. free market-based system. Whether that is a prudent policy, and whether pharmaceutical manufacturers—or third-party middlemen—are ultimately responsible for U.S. prescription drug prices, is beyond the scope of this comment letter. But regardless of the wisdom of the underlying policy, and the potential impact on the U.S. economy, Congress clearly and expressly provided important boundaries in the IRA, and CMS in its Initial Memorandum has egregiously exceeded what Congress intended. We are particularly concerned with the overly broad QSSD definition which, as we have explained, subjects Part B drugs to an MFP-based reimbursement rate in IPAY 2026, jeopardizing patient access to these Part B therapies—a result CMS did not foresee as it sought to advance overly zealous policy goals.

CMS must reconsider and revise key operative portions of the Initial Memorandum, including Section 30. United Therapeutics hopes that CMS understands the magnitude of the responsibility given to it by Congress under the IRA: The mere publication of a drug on the selected drug list is likely to immediately cause dislocations in the pharmaceutical market, long

before an MFP is even published. CMS must understand that the U.S. pharmaceutical industry and marketplace are not separate from, or adverse to, patients and Medicare beneficiaries—they are one and the same. Damage to the U.S. pharmaceutical industry and its ability to provide medical innovation directly translates into patients losing access to existing therapies or never having the chance to receive new therapies, because the avenue for bringing them to market has been foreclosed.

Sincerely,

A handwritten signature in black ink, appearing to read "Kevin T. Gray". The signature is fluid and cursive, with a large initial "K" and a stylized "G".

Kevin Gray
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April 13, 2023

Meena Seshamani, M.D., Ph.D.
Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services (CMS)
Baltimore, MD

SUBJECT: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of
Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026

RE: Solicitation of Comments

Dear Dr. Seshamani,

On March 15, 2023, the Centers for Medicare & Medicaid Services (CMS) released draft guidance on how the agency will implement the drug price negotiation provisions of the Inflation Reduction Act. The following comments and recommendations are specific to section 60.3, “Methodology for Developing an Initial Offer.” As CMS moves forward with the first round of negotiations, the team reviewing each drug will need to aggregate a wide range of comparative effectiveness evidence and manufacturer-submitted data to arrive at a preliminary price offer. Importantly, evidence on comparative effectiveness will encompass typical surrogate or primary endpoints from clinical trials, patient experience and preferences, and broader contextual factors (e.g., whether the drug targets severe conditions) that may be important to our values as a society. Some evidence may be quantifiable (e.g., incremental change in a primary endpoint versus therapeutic alternative) whereas other evidence may be more difficult to quantify (e.g., patient experience factors). Some evidence that cannot be quantified may hold more importance for patients, families, providers, payers, and policy-makers than typical primary endpoints from clinical trials.¹

Our team has studied decision-making processes where multiple sources of evidence – both quantitative and qualitative – can be combined in to one framework to facilitate the evaluation of a therapy and inform decision-making around pharmaceutical coverage or pricing. We believe this type of framework could be used by CMS to guide the development of the preliminary price as described in sections 60.3.3 and 60.3.4. In this comment, we provide two main recommendations related to using a structured framework for evaluating multiple, often conflicting factors, on a drug’s risks, benefits, and costs. But first we provide a brief discussion of terminology.

CMS states in section 60.3.3 that it considered both a quantitative and qualitative approach for adjusting the starting point for an initial offer and ultimately proposed a qualitative approach. In the recommendations below, we do not rely on the quantitative versus qualitative distinction and instead refer to our proposed approach as ‘structured deliberation’. We prefer this terminology for two reasons. First, describing approaches to evidence aggregation as quantitative versus

¹ Trenaman L, Pearson SD, Hoch JS. How Are Incremental Cost-Effectiveness, Contextual Considerations, and Other Benefits Viewed in Health Technology Assessment Recommendations in the United States? Value Health. 2020 May;23(5):576-584.

qualitative may introduce confusion when also discussing quantitative versus qualitative evidence. Second, we believe the best approaches to evidence aggregation are likely to integrate both quantitative (e.g. numerical weights and scores) and qualitative elements (e.g. deliberation between stakeholders and flexible, non-algorithmic decision-making).² Finally, we use the term aggregation to refer to identification, grouping, prioritization, and scoring of both quantitative and qualitative evidence on a selected drug for a particular indication. Given the identification process has largely been implemented in the CMS guidance, our recommendations below refer to subsequent steps of aggregation.

Recommendation 1: To account for both quantitative and qualitative evidence, we recommend that CMS use an existing framework to group and prioritize all the evidence sources and factors that may inform the negotiation process.

The framework we developed groups and prioritizes information in a way that can generalize across all negotiable drugs but also provide flexibility in allowing situation-specific factors to be included in the decision-making process. In particular, and as noted in the guidance, CMS will consider a variety of factors and evidence sources to determine a preliminary price for negotiations yet have not stated the level of importance they may place on different evidence types, including quantitative versus qualitative evidence. We recommend CMS facilitate a structured deliberative process each calendar year to group and prioritize evidence on these factors to inform the initial offer and subsequent negotiations. Our team developed the first of its kind structured deliberation format that includes generation of a priority list of factors important to decision-making in multiple contexts including important aspects of treatments to patients and their families, providers, payers, and other stakeholders. The method we developed facilitates voting panel members to prioritize factors at a group level, where each person's opinion is counted. This method also supports a structured form of group-level deliberation allowing for the inclusion of factors that are less quantifiable but represent concepts important to patients and their families, providers, payers, and other stakeholders. The method is pragmatic and flexible, supporting efficient updates when preferences change or new factors are included in the process.

We tested our framework with the Colorado Prescription Drug Affordability Board in addition to multiple stakeholders - e.g., patients with a particular disease to identify the importance of patient experience factors and multi-stakeholder groups to identify the importance of societal contextual factors.³ Our findings suggest: 1) using a structured framework facilitates deliberations on both qualitative and quantitative evidence in a transparent and efficient manner; 2) consistency, predictability, and prioritization will influence activity on evidence generation either by value assessors or by stakeholders informing value assessment (industry, clinical guidelines, patient advocates, etc.); and 3) the method of prioritization we created is reproducible, efficient in hybrid, online, or in-person approaches (e.g., completed within 2-3 hours), and can be applied to prioritize any valued factors, not just the factors required through legislation.

² DiStefano MJ, Krubiner CB. Beyond the numbers: a critique of quantitative multi-criteria decision analysis. *Int J Technol Assess Health Care*. 2020;36(4):292-296.

³ [Prescription Drug Affordability Review Board | DORA Division of Insurance \(colorado.gov\)](https://www.colorado.gov/prescription-drug-affordability-review-board); March 31, 2023 meeting and prioritization exercise; McQueen RB, Mendola ND, Jakab I, Bennett J, Nair KV, Németh B, Inotai A, Kaló Z. Framework for Patient Experience Value Elements in Rare Disease: A Case Study Demonstrating the Applicability of Combined Qualitative and Quantitative Methods. *Pharmacoecoon Open*. 2023 Mar;7(2):217-228.

Recommendation 2: Within the framework, group factors into “domains” that can be weighed by order of importance to patients and their families, providers, payers, and other stakeholders.

After reviewing the CMS guidance, we propose grouping factors in to three separate domains that represent large categories of evidence: 1) therapeutic advancement (e.g., clinically significant change in primary endpoint versus comparator); 2) patient and caregiver experience factors (e.g., drug reduces caregiver burden); and 3) societal and system-level factors (e.g., drug will result in system-level cost savings). Within each domain, there may be multiple factors that are important to the determination of the preliminary price. But regardless of how the factors are grouped into domains, CMS can weigh the factors in a way that incentivizes evidence generation and submissions with the opportunity for therapies to be “scored” on each factor. The process of weighing each domain and factor within each domain is a standalone process that helps facilitate a transparent discussion among stakeholders about important aspects of evaluating therapies. A further step including “performance scores” may allow for therapies to be scored for their benefits on both quantitative and qualitative evidence submissions. If the weights are combined with performance scores for each therapy, these results may be used as a modifier on negotiated price options. For example, if the drug is highly beneficial not only in terms of its primary endpoint, but also on patient experience factors (e.g., oral route of administration vs infusion) and issues impacting broader society (e.g., addressing an unmet medical need), this framework would help account for those additional factors in the maximum fair price negotiation. The framework is also very flexible with no scoring algorithm used as a modifier. Simply weighing the domains and factors improves transparency and incentivizes evidence generation and submissions from external stakeholders along with internal CMS-led evidence reviews. This allows rapid updates, for example, if the manufacturer brings additional evidence of therapeutic benefit or an additional factor for consideration to a negotiation meeting.

We applaud CMS for undertaking the difficult process of aggregating multiple factors to inform a preliminary negotiation price. As a team, we understand the nuances of mixed methods approaches and our framework will be helpful for CMS in multiple areas of the negotiation process. Please do not hesitate to reach out to our team for any advice or guidance on implementing our proposed process. Thank you for your time reading our comments.

Sincerely,

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April 14, 2023

VIA Electronic Filing – IRARebateandNegotiation@cms.hhs.gov

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RE: Response to “Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments” - Developing Continuous Patient Engagement to Support the Medicare Drug Price Negotiation Program

Dear Dr. Seshamani:

We are writing to comment on the March 15 draft guidance released by the Centers for Medicare & Medicaid Services (CMS) on implementing the Medicare Drug Price Negotiation Program (DPNP). We appreciate CMS providing this important mechanism for input and urge the agency to establish and apply a patient-centered approach to its negotiation process and factors. A patient-centered approach would ensure that the development of the DPNP “formally includes a range of outcomes and data sources—including those related to patient and caregiver experiences—that are foundational to patient-centeredness, so that the implementation of Medicare drug benefits better aligns with the goals of patients they were designed to serve.”¹ The inclusion and representation of patients and stakeholder are critical to improving health care outcomes, quality, safety, and access in the United States.

Failure to engage patient communities meaningfully would represent an avoidable misstep by CMS as these stakeholders bring unique and essential expertise and perspectives on the value of medicines. Their firsthand experience with the selected drugs, therapeutic alternatives, and the medical system in a real-world setting is essential to consider while conducting healthcare research. Academics, thought leaders, and research organizations have underscored the importance of including patient and caregiver input in evidence-based processes.

The initial guidance document left us with questions regarding how patients or caregivers’ perspectives will be meaningfully considered in the implementation of the DPNP and how their input will be sought throughout the process as described in the guidance. For example, CMS notes that the public will have an opportunity to submit data through an Information Collection Request beginning after the announcement of the selected drugs. The 30-day window afforded stakeholders to offer input after the list of selected drugs is published on September 1st may not be enough time for patients, providers, or caregivers to gather and submit data. We hope that

¹ Mattingly, TJ and Mullins CD. [Achieving Patient-Centeredness In Medicare’s New Drug Price Negotiation Program](#). *Health Affairs Forefront*. 2023.

CMS will revise the guidance and explicitly create formal methods to engage key stakeholders throughout the process.

This comment letter also serves to notify you of an upcoming research project designed to incorporate the expertise of The PATIENTS Professors Academy graduates to provide suggestions to improve how CMS engages stakeholders in the DPNP using the 10-Step Framework for continuous patient and stakeholder engagement.² (*Shown in Appendix Figure A1*). We hope this project can offer insights to CMS on optimal opportunities to work with the patient communities to improve the negotiation process. We eagerly welcome CMS's partnership on this project to ensure it can appropriately inform its goals. We intend to provide insight directly from patients trained in applying this Framework who each bring their own lived experiences and perspectives to the engagement process.

As researchers in patient engagement and patient-centered decision-making, the PATIENTS Program and Applied Patient Experience, LLC are organizations devoted to ensuring continuous and authentic engagement with patient populations throughout the research life cycle. CMS needs to ensure that disease-specific patient-community perspectives are accounted for when evaluating the clinical benefits of selected medicines. However, patient perspectives can only be meaningfully considered if engagement occurs early and throughout the process to identify and assess data and determine how the data are weighted and used in CMS decision making. As such, we call on CMS to adopt a proactive, formalized approach to engaging patients.

The PATIENTS Program is an interdisciplinary research team of community partners and researchers based out of the University of Maryland Baltimore's School of Pharmacy. The PATIENTS Program provides a proven approach to continuous engagement in patient-centered research, known as the 10-Step Framework for Continuous Patient Engagement. Since 2013, the PATIENTS Program has served as a bridge between West Baltimore communities and researchers at the University of Maryland Baltimore. The shared vision is that "patients and stakeholders are heard, inspired, and empowered to codevelop research." The benefits of the approach include (1) an authentic commitment to—and from—the community, (2) faster recruitment and greater retention in studies; (3) enhanced diversity for representative results; and (4) better patient self-management because of the inclusivity in research. The PATIENTS Program is housed within the Department of Practice, Sciences, and Health Outcomes Research (P-SHOR) at the University of Maryland, Baltimore, which improves health care through innovation, collaboration, and advocacy to achieve excellence in pharmacy education, practice, and research. There are more than 50 faculty members whose training and expertise encompass pharmacy, public health, pharmacoepidemiology, pharmacoconomics, health services research, law, and health policy. The health services and outcomes research initiatives promote health services and outcomes research and advance information on public policy and health outcomes related to prescription drug use and delivery. It advocates advanced education and research training in behavioral, economic, and epidemiological/pharmacoepidemiologic health services and policy analysis as applied to drug use and distribution problems. P-SHOR addresses these goals by:

- Conducting new and innovative research related to the delivery, use, costs, and safety of pharmaceuticals and other healthcare products

² Mullins CD, Abdulhalim AM, Lavallee DC. [Continuous Patient Engagement in Comparative Effectiveness Research](#). JAMA. 2012. and Edwards HA, Huang J, Jansky L, Mullins CD. [What Works When: Mapping Patient and Stakeholder Engagement Methods Along the Ten-Step Continuum Framework](#). Journal of Comparative Effectiveness Research. 2021.

- Providing expertise, support, and leadership to professional, governmental, community, and health-related organizations and agencies
- Training graduate students, post and pre-doctoral fellows for future academic, industry, and public policy positions through a variety of academic, training, and mentoring programs

The PATIENTS Program provides a proven approach to continuous engagement in patient-centered research across multiple medical specialties. In 2022, the PATIENTS Program launched its **PATIENTS Professors Academy**. This free 5-week virtual program teaches the PATIENTS Program 10-Step Framework for continuous patient and stakeholder engagement with interactive components led by patient advisors and subject matter experts. Research is conceptualized and driven by communities of patients and their care providers. In 2022, the Academy graduated 90 “Professors”. Graduates of The PATIENTS Professors Academy are able to advise companies, government agencies, community-academic partnerships, and other entities on ways to make clinical and translational research more relevant, appealing, and diverse.

Applied Patient Experience, LLC is a patient engagement and patient-centered research consulting firm. Our expertise is engaging individuals and their caregivers about their experiences living with a disease or disability and applying those insights to guide decisions across drug development, value/health technology assessment, and real-world studies. We provide advisory services and conduct high-quality patient-centered research in partnership with non-profits, government, life science, and technology companies.

We would be happy to engage you to determine where our research could be most impactful or to describe our process in greater detail. After our research concludes, we will share our final report and be accessible to the team at CMS should there be an opportunity to provide clarifications or additional details.

We appreciate the opportunity to provide comments on the draft guidance. Please get in touch with any of the project leadership below if you have questions. We hope to continue to engage with CMS on the issue of patient engagement in the application of the IRA.

Sincerely,



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Elisabeth M. Oehrlein, PhD, MS
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Joseph E. Vandigo, MBA, PhD
Principal Scientist & Director of Value
Applied Patient Experience, LLC.

Appendix.

Figure A1. Enhancement of Comparative Effectiveness Research (CER) Through Continuous Patient Engagement. (*As originally published in JAMA, August 2012*)

Figure. Enhancement of Comparative Effectiveness Research (CER) Through Continuous Patient Engagement

Step in CER Process	Purpose of Patient Engagement
Topic solicitation	<ul style="list-style-type: none"> ■ Identify topics that are important to patients, caregivers, and the community ■ Propose topics to be investigated
Prioritization	<ul style="list-style-type: none"> ■ Solicit feedback on relevance and priority of topics ■ Discuss the urgency of addressing topics
Framing the question	<ul style="list-style-type: none"> ■ Ascertain questions' relevance and usefulness ■ Assess "real-world" applicability
Selection of comparators and outcomes	<ul style="list-style-type: none"> ■ Identify comparator treatments of interest ■ Identify outcomes of interest ■ Incorporate other aspects of treatment
Creation of conceptual framework	<ul style="list-style-type: none"> ■ Provide a "reality check" ■ Verify logic of conceptual framework ■ Supplement with additional factors not documented in the literature
Analysis plan	<ul style="list-style-type: none"> ■ Verify importance of factors and variables ■ Ascertain whether there is a good proxy for a specific concept ■ Inquire about potential confounding factors
Data collection	<ul style="list-style-type: none"> ■ Determine best approaches for data collection (eg, trial, registry, medical charts) ■ Assist with selection of data sources
Reviewing and interpreting results	<ul style="list-style-type: none"> ■ Assess believability of results ■ Suggest alternative explanations or approaches ■ Provide input for sensitivity analysis
Translation	<ul style="list-style-type: none"> ■ Interpret results to be meaningful ■ Document which results are easy or difficult to understand ■ Indicate which results are counterintuitive
Dissemination	<ul style="list-style-type: none"> ■ Facilitate engagement of other patients ■ Help other patients to understand findings

April 13, 2023

Meena Seshamani, M.D., Ph.D.

CMS Deputy Administrator and Director of the Center for Medicare

Centers for Medicare & Medicaid Services

U.S. Department of Health and Human Services

7500 Security Boulevard

Baltimore, MD 21244-8016

Attn: PO Box 8016

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Seshamani:

Thank you for the opportunity to submit comments on the Center for Medicare & Medicaid Services' (CMS) initial guidance, *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments* ("initial guidance").¹ I am a Professor of Internal Medicine in the School of Medicine and a Professor of Health Management and Policy in the School of Public Health at the University of Michigan and where I direct the Center for Value-Based Insurance Design ("VBID Center"). My three-decade research and policy agenda focuses on increasing access to, and enhancing equity in the delivery of essential clinical services.

The Inflation Reduction Act's provisions on prescription medicines are of seminal importance to American health care. The law establishes, for the first time, a cap on patient's out-of-pocket costs in Medicare Part D and allows Part D enrollees the option to make cost-sharing up to the out-of-pocket maximum more affordable by electing a maximum monthly cap that spreads cost-sharing across the year. These provisions address significant problems in patient affordability of medicines. As a colleague and I have written, "There is immediate urgency to provide patients with relief from out-of-pocket costs for their medications.... A robust evidence base confirms that medication adherence declines as patients are required to pay more to fill their prescriptions."²

Another part of the law, establishing CMS negotiation of certain Medicare Part B and Part D drug prices, is also profoundly important to U.S. health care. Medicare's large share of the U.S. market means that the program's determination of selected drugs' program-wide "Maximum Fair Price" (MFP) will play a large role in establishing incentives for manufacturers of brand medicines. These

¹ <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>

² http://vbidcenter.org/wp-content/uploads/2019/01/AJMC_02_2019_Fendrick-1-22-19.pdf

² http://vbidcenter.org/wp-content/uploads/2019/01/AJMC_02_2019_Fendrick-1-22-19.pdf

decisions by the Secretary of Health and Human Services (HHS) invariably will affect which medicines and which indications for medicines brand manufacturers pursue and which they sideline, the timing of development and even the timing of availability on the U.S. market. Further, physicians, patients and caregivers represent important stakeholders in this program,³ and the process and standards the agency establishes will set an important benchmark for consideration of clinical factors and physician input in its decision-making.

One facet of the VBID Center's work has centered on the concept of "clinical nuance" recognizing that 1) medical services differ in the amount of health produced, and 2) the clinical benefit derived from a specific service depends on the consumer using it, as well as when, where, and by whom the service is provided."⁴ Another facet of the work done at VBID Center has recognized that the emergence of precision medicines means, in certain circumstances defined by clinical criteria, what has been conventionally treated as "the first-line therapy is no longer high-value, and a clinically indicated, 'precision' alternative becomes a higher value choice."⁵ Both areas underscore the need for multi-faceted, nuanced assessments of clinical factors and circumstances when making policy choices, especially those pertaining to affordability of medications

No medical service or medication is always high or low value, but depends on factors such as the patient and the specific clinical scenario. The MFP statute appears to recognize this point, directing the agency to consider the effects of treatments on various patient populations. The initial guidance further reinforces that similar multi-faceted, granular assessments of clinical factors and circumstances are demanded in Part D price negotiation. This approach requires well-structured input from expert clinicians to define the analyses that will be conducted and to evaluate and draw conclusions from the evidence they generate.

Following the statute, the initial guidance identifies multiple parts of setting the MFP that turn on clinical determinations, with each specific to a particular indication of a given drug. These include, for instance, selecting the therapeutic alternative, outcomes considered, determining the comparative effectiveness of the drug and whether the drug represents a therapeutic advance or addresses an unmet need.

CMS's reviews of drug- and indication-specific assessments inevitably will involve analysts with a variety of backgrounds and skills synthesizing and reaching judgments based on a large volume of complex information. However, the specific, nuanced clinical determinations that the initial guidance designates as central to determining the MFP *make it particularly important that appropriate clinical expertise be engaged on each clinical question.*

In this context, appropriate clinical expertise requires well-structured input throughout the process from clinicians who regularly treat patients with the conditions for which the

³ <https://www.healthaffairs.org/content/forefront/implementing-drug-negotiation-provisions-ira-considerations-cms>

⁴ <https://vbidcenter.org/wp-content/uploads/2017/03/Precision-Medicine-1-pager-1-15-20.pdf>

⁵ Ibid.

drug/indication is prescribed.⁶ Data, studies and other evidence cannot be properly used to address the clinical questions CMS has specified without a system for obtaining expert clinicians' advice in defining the questions and evaluation of the evidence. This is needed to draw upon specific knowledge about illnesses and treatments that may not be embedded in studies, yet must play an important role in the agency's decisions. It also is needed to bring real world experience to interpreting and making judgments about data, including clinical nuance that will not necessarily be evident to non-clinicians or to clinicians who are not expert in currently treating patients for the disease/indication at issue. Experienced clinicians do not have the only relevant skills for the assessments and decisions CMS has described but these determinations about "nuanced differences between drugs" cannot be properly made without their skills.

The single, 30-day "information collection request" proposed by CMS at the start of the drug-specific MFP process may not be sufficient for obtaining the expert clinical input needed by the agency. CMS should make targeted revisions to its initial guidance to ensure that the agency is obtaining the expert engagement needed on clinically relevant determinations as called for in the initial guidance and listed above.

Essential points for CMS to obtain clinician input will occur at the start of the process, during the process when initial draft MFP decisions are proposed, and at the end of the process when CMS must publish MFP explanations. These key points for engagement are described in more detail below:

- 1) **Early in the MFP decision-making process**, CMS must establish procedures for earlier, more robust engagement with clinical experts. A single, broad solicitation for input, while a good initial step, may not be sufficient to serve this purpose.
- 2) **During the MFP process**, CMS should seek physician and expert clinical input on the research and evidence synthesis it is relying on in its review, how it is weighting evidence and outcomes, and how it proposes to consider patient differences and clinical nuance across indications and patient subgroups,
- 3) **After publication of CMS' explanation of each selected drug's final MFP**. The law requires CMS to publish a summary explanation of how it came to the final MFP several months after the MFP decision itself is made and published. CMS should ensure that these explanations provide enough detail for clinical experts to be able to see how their input was or was not considered in the agency's final decision. The publication of the explanation should occur in a timely enough manner so that clinical experts can see and learn from how their input was considered before the process begins for the next year of selected products. In addition, CMS should solicit public comment, including from clinical advisors and/or practicing physicians, in order to foster agency learning and continuous improvement of the MFP program.

⁶ Because it is the clinical experts who have the relevant expertise, it is important that assessments and conclusions be prepared and structured by them rather than by staff or contractors without such expertise.

There are a number of methods by which CMS can obtain clinician input. For example, CMS could establish therapeutic area-specific Clinician Advisory Panels that are focused on guiding clinically relevant decision making for each selected product. The Panels should include multiple physicians who regularly treat patients for the conditions/indications for which the selected drug is prescribed. Panel members could be selected following consultation with the relevant medical specialty societies and organizations representing patients and, to assure neutrality, be mutually acceptable to CMS and the manufacturer. They should also reflect the range of practice settings and types of patients with the condition.

In its initial guidance, CMS has recognized the important principles of evaluating drugs based on their clinical performance and that such an evaluation must be conducted with attention to nuanced differences between drugs. Operationalizing these principles in a single determination that applies across 50 million seniors and disabled persons is especially challenging. Establishing a system that provides for neutral clinical experts to fully inform the clinical questions, data and conclusions specified in the initial guidance is one element of meeting the challenge.

Finally, while I am hopeful that the provisions of the law to redesign Part D will positively impact beneficiary access to needed medicines, as stated above, I am concerned that *unintended formulary effects of introducing a drug whose price is restricted to the MFP may alter incentives for how well plans cover other agents in the same therapeutic class*. Over time, plans have increasingly imposed formulary controls such as utilization management and formulary exclusions. When an MFP is identified, I have concern that these existing formulary management tools will intensify. *As such, CMS should regularly monitor plan formularies to ensure access is not increasingly restricted.*

Lastly, while the law requires that beneficiary cost sharing be based on the MFP for selected drugs, this cost sharing based on net price does not extend to all medicines in Part D. CMS should move to redefine negotiated price in Part D to factor in discounts and rebates, to provide parity in cost sharing rules for beneficiaries using non-MFP medicines. Patient access to therapeutic options in recognition of clinical nuance should be the top priority for CMS as these provisions are implemented.

Thank you for the opportunity to comment on this important policy. I applaud your many efforts aimed to enhance access and affordability to essential medications for Medicare beneficiaries. Please feel free to call on me if I can assist you in any way.

Sincerely,



A. Mark Fendrick, M.D.

Director, University of Michigan Center for Value-Based Insurance Design
Professor, Internal Medicine and Health Management & Policy

April 14, 2023

Meena Seshamani, M.D., Ph.D.

Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services (CMS)
Baltimore, MD

RE: Response to Solicitation for Comments, Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026

Dear Dr. Seshamani,

Thank you for the opportunity to comment* on the Medicare Drug Price Negotiation Program. As researchers with expertise in pharmacoeconomics, health economics and policy, we have been studying trends in drug pricing and payment models in order to improve patient access to effective treatments, while creating incentives for U.S. manufacturers of health technologies to continue innovating. Our comments draw on our experiences and per developed in that research. We share a mission to measurably improve the value for money accruing from pharmaceuticals and other health technologies, through evidence-based policy solutions, research excellence, and public-private partnerships.

As CMS begins building a new program that relies in part on health economic principles to implement the Medicare Drug Price Negotiation Program, we recommend incorporating several key elements to promote the program's success. Our recommendations have the goal of building public confidence and stakeholder buy-in through rigor and reliable application to CMS decision-making. As described in greater detail below, we recommend that CMS:

- Establish explicit methodological standards to ensure the rigor of research, evidence reviews, and assessments;
- Describe a methodology for applying evidence to pricing decisions that places the greatest weight on added clinical benefit and contextual factors, such as unmet medical need;
- Create a transparent process to:
 - a. solicit input from patients, physicians, and academic researchers with expertise on issues such as choice of comparators and outcomes;
 - b. describe to stakeholders how they are their input will be considered in proposed decisions.

Therefore, we provide the following comments and that we believe would be helpful to consider as your office continues to advance efforts for Drug Price Negotiation through the Medicare Program:

1. **Current CMS Position:** *Apply adjustments by the manufacturer-specific factors outlined in the law to determine the initial offer price.*

Our Recommendation: Place greater emphasis on the clinical benefit factors (e.g. survival, rate of cure), as prioritized with input from the patient community affected, rather than manufacturer-specific factors. Manufacturer-specific factors would lean more towards a cost-plus pricing model, which rewards less efficient firms rather than those providing the most benefit to patients. This is particularly important given vertical integration of PBMs, insurers and pharmacies, which already have an incentive to share data with their rebate-conferring drug company partners. These will be the only entities controlling this essential information, which is necessary for evaluating the drug company's value claims. Such information and data analytic asymmetries will only expand and grow more problematic, making it nearly impossible for payors and government entities to engage in independent auditing.

In contrast, a clinical benefit factor-based negotiation process provides CMS with the ability to reward efficiency and clinical benefit, which ultimately reduces costs and benefit patients. Transparent incorporation of benefits will lead to pricing models that align better with the value of the technology to Medicare beneficiaries and American taxpayers.

2. **Current CMS Position:** *Engage members of the public (including people with Medicare, consumer advocates, prescription drug companies, Medicare Advantage and Part D plans, health care providers and pharmacies, and other interested parties) on key policies, make requests for information, and inform the public on other implementation timelines and milestones.*

Our Recommendation: A stakeholder engagement process should provide input on the priorities and activities of the drug price negotiation methodology and decision-making.¹ Adopt a deliberative, continuous, and transparent process to engage the stakeholders (i.e., those mentioned above in your current position) *as well as* patients affected by the treatments under review, experts in pharmacoeconomics, health economics, and outcomes research and policy. These experts have diverse perspectives to identify and evaluate evidence that can provide insight into the negotiation process that the other listed stakeholders may lack.

¹ Lakdawalla DN, Neumann PJ, Wilensky GR. Health Technology Assessment in the U.S. – A Vision for the Future. Los Angeles: USC Schaeffer Center, 2021. Accessed at: <https://healthpolicy.usc.edu/research/health-technology-assessment-in-the-u-s-a-vision-for-the-future/>.

3. **Current CMS Position:** *CMS intends to consider health outcomes, intermediate outcomes, surrogate endpoints, patient-reported outcomes, and patient experience when reviewing the clinical benefit of the selected drugs and its therapeutic alternative(s).*

Our Recommendation: Ensure evidence on clinical benefit and unmet need reflects perspectives and experiences important to patients, as well as their caregivers, clinicians, and society, including selection of therapeutic alternatives, outcomes, and unmet needs. Given variation in evidence sources, weight should be applied to those factors most important to patients, caregivers, clinicians, and society. CMS can leverage real-world data (e.g., payer claims, patient registries, and electronic health records) and patient-centered outcomes research (e.g., mixed-methods) approaches to capture this information. There are multiple frameworks available to incorporate multi-stakeholder perspectives.²

In addition, we encourage CMS to evaluate the potential role for measurements of value beyond clinical benefit and unmet need. We recognize that the Inflation Reduction Act creates some limitation to this by focusing on comparative effectiveness research and mandatory ceiling price discounts unconnected to value measurement, but we also believe that any price negotiation should be conducted transparently and linked to a drug's value for money to the extent possible.³ While the Affordable Care Act, and Inflation Reduction Act, have prohibited the use of traditional economic measures of value, such as the quality-adjusted life year (QALY), because they assign less value to life extensions for patients with disability and severe disease, recent advances in value assessment may provide alternative pathways forward. For example, the Generalized Risk-adjusted Cost-Effectiveness (GRACE) framework offers an empirical pathway to evaluating price relative to value for all patients without bias for inequities.⁴ CMS should launch a dialogue with relevant stakeholders to discuss potential approaches to broader consideration of value measures, consistent with past recommendations of several expert panels.^{1,3,5}

² McQueen RB, Mendola ND, Jakab I, Bennett J, Nair KV, Nmeth B, Inotai A, Kal Z. Framework for Patient Experience Value Elements in Rare Disease: A Case Study Demonstrating the Applicability of Combined Qualitative and Quantitative Methods. *Pharmacoecon Open*. 2023 Mar;7(2):217-228.

³ Goldman DG, Grogan G, Lakdawalla D, Liden B, Shafrin J, Than KS, Trish E. Mitigating the Inflation Reduction Act's Potential Adverse Impacts on the Prescription Drug Market. Schaeffer Center White Paper Series. Los Angeles: Leonard D. Schaeffer for Health Policy & Economics, April 2023.

⁴ Lakdawalla DN, Phelps CE. Health Technology Assessment With Diminishing Returns to Health: The Generalized Risk-Adjusted Cost-Effectiveness (GRACE) Approach. *Value Health*. 2021 Feb;24(2):244-249. doi: 1.116/j.jval.22.13. Epub 221 Jan 12. PMID: 3351831.

⁵ Rimber BK, Harper H, Witte ON. Promoting Value, Affordability and Innovation in Cancer Drug Treatment. A Report from the President of the United States from the President's Cancer Panel. Bethesda, MD: President's Cancer Panel; 218 March.

4. **Current CMS Position:** *CMS intends to consider the source, rigor of the study methodology, current relevance to the selected drug and its therapeutic alternative(s), whether the study has been through peer-review, study limitations and degree of uncertainty of conclusions, to ensure integrity of the contributing data within the negotiation process (page 37).*

Our Recommendation: Establish rigorous and more detailed standards for evidence relied upon in both the literature review and all third-party submitted data, as well as CMS's own "internal analytics." While CMS indicates that it intends to employ rigorous standards, CMS does not indicate what these standards will be, what methods will be used to establish them, or if they will apply to internal analyses conducted by CMS. Other organizations, including the International Society for Pharmacoeconomics & Outcomes Research (ISPOR), the International Society for Pharmacoepidemiology (ISPE), and a recent Health Technology Assessment Panel Report co-published by the Aspen Institute and USC Schaeffer Center provide specific guidance on methods that are rigorous and could apply to drug price negotiation analytics.

5. **Current CMS Position:** *CMS intends for the published explanation of Maximum Fair Price (MFP) to summarize how relevant negotiation factors were considered during the negotiation process.*

Our Recommendation: The explanation of Maximum Fair Price (MFP) should be thorough and released as early as possible to enhance the predictability and transparency of the process. Such thoroughness should specify that CMS will include in its public announcement of the MFP:

- How it selected the therapeutic alternatives;
- How the various factors were weighed;
- How stakeholders were engaged;
- How evidence was considered;
- How types of outcomes were considered;
- How unmet need was defined;
- And, which priority populations were considered.

Thank you for your time and consideration of these issues as we as a nation continue to explore the programmatic structure of Medical Drug Price Negotiation.

Sincerely,

Dana P. Goldman, PhD
Dean & Distinguished Professor of Public Policy, Pharmacy, and Economics
C. Erwin & Ione L. Piper Chair
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**The information contained in this letter to CMS represents the ideas and opinions of the signed individuals, and does not necessarily represent the positions of their home institutions – Geisel School of Medicine at Dartmouth, Johns Hopkins Bloomberg School of Public Health, Pennsylvania State University, Tufts University, University of Chicago, University of Colorado, University of Maryland School of Pharmacy, University of Rochester, University of Southern California, USC Leonard D. Schaeffer Center for Health Policy & Economics, University of Utah, University of Washington, Virginia Commonwealth University.*



April 14, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
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IRAREbateandNegotiation@cms.hhs.gov

Re: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure,

Ventus Therapeutics ("Ventus") appreciates the opportunity to submit comments in response to the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments posted on the Centers for Medicare & Medicaid Services (CMS) website on March 15, 2023 (Drug Price Negotiation Program Guidance).

Ventus is a U.S.-based biopharmaceutical company founded in 2019 with the mission to create exceptional small molecule medicines for seriously ill patients. Our proprietary drug discovery platform, ReSOLVE™, gives us unique insights into the molecular structure of disease-causing protein targets to guide the development of differentiated therapies at a fast pace. Ventus is specifically focused on accessing important disease targets with small molecules. Our lead drug candidates include a potential first-in-class and a potential best-in-class medication for the treatment of diseases of systemic inflammation and neuroinflammation, respectively. Systemic inflammation drives the burden of patients suffering from a wide range of severe diseases, such as lupus, systemic sclerosis, dermatomyositis, and osteoarthritis, among many others. Neuroinflammation is the hallmark of many diseases related to aging, such as Alzheimer's disease and Parkinson's disease. Strong preclinical data demonstrate the potential efficacy of our programs in several of these diseases. In addition, many of these diseases continue to have significant unmet need where millions of patients have no good treatment options available today. Investment in the development of innovative and novel therapies, such as those in Ventus' pipeline, is required to improve the lives of patients suffering from these diseases.

Ventus recognizes that the CMS has a tremendous task ahead to implement the Inflation Reduction Act (IRA). We also understand that CMS considers its guidance on Section 30 to be final. However, given the fact that Ventus recognizes the importance of developing affordable medications, we highlight the importance of small molecules as a therapeutic modality that should be part of the solution and not penalized. Section 30, as written, would have a significantly negative impact on the funding of important research and development efforts for diseases of the elderly, such as Alzheimer's disease, cancer, and blindness, by disproportionately penalizing small molecule drugs. For these reasons, we are including our comments below, which we would have made had comments been permitted.

Section 30.1:

Medicare price negotiation of NDA-path drugs at seven-years from the date of approval significantly degrades the availability of funding for the development of small molecule drugs for age-related diseases, such as Alzheimer's disease.

Small molecules represent the most tried, tested, and proven modality among all drug modalities in development today. Other modalities, such as antibodies, gene therapies, and cell therapies, have many disadvantages compared to small molecules: they are significantly more expensive to manufacture, add more cost to the overall health system (i.e., infusion costs, need for special equipment to deliver the drugs, etc.), and, for certain modalities, are much less proven with more safety liabilities. In addition, patients of all ages, especially elderly patients, prefer the convenience of an oral small molecule. Small molecules are trusted by the public, who often mistrust different therapeutic modalities, as recently seen during the COVID epidemic.

What is not so different between NDA-path drugs and BLA-path drugs is the research and development of both types of drugs. There is no meaningful cost difference between developing a small molecule or a biologic. In addition, because small molecules are generally easy to genericize, prices for these drugs typically drop by approximately 80-90% or more when patent exclusivity ends and one or more generics enter the market, which is much more significant than seen with biosimilars or other modalities. Furthermore, the probability of success (or failure) is the same, regardless of modality.

Significantly disincentivizing the development of small molecules for diseases of the elderly, despite small molecules being no different than biologics from a development cost, risk, or timeline perspective, runs counter to the overarching goals of the IRA in terms of driving affordability in the long-term for Medicare patients. And the long-term impact of this disincentive will be substantially fewer small molecules developed and approved for chronic and highly prevalent diseases affecting the elderly population. This would then lead to reduced treatment options, increased number of injections, and higher cost of care for patients, payers, and society.

Our recommendation: Revise the eligibility period for price negotiations for small molecules to match the 11 years set for large molecule drugs. This increase of four years will preserve most incentives to develop novel small molecule drugs and ensure that all drugs essentially “go generic” without undue delay, putting an end to wasted spending.

* * * * *

We appreciate your consideration of our comments as you develop the Drug Price Negotiation Program policy. We look forward to continuing to work with CMS to ensure that this program is implemented in a manner that minimizes the potential harm to seniors from fewer innovative medicines. Please contact our V.P., Intellectual Property & Legal, Dr. Robin Weatherhead, at RWeatherhead@ventustx.com for questions and comments relating to this letter. We would welcome the opportunity to meet with you or answer any questions CMS may have about our comments, at your request.

Sincerely,

Marcelo E. Bigal

Marcelo Bigal, M.D., Ph.D.
President & Chief Executive Officer
Ventus Therapeutics



April 14, 2023

Via electronic submission: IRARebateandNegotiation@cms.hhs.gov

Meena Seshamani, M.D., Ph.D.

CMS Deputy Administrator and Director of the Center for Medicare

Centers for Medicare & Medicaid Services

U.S. Department of Health and Human Services

7500 Security Boulevard

Baltimore, MD 21244-8016

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Administrator Seshamani:

ViiV Healthcare Company (ViiV) appreciates the opportunity to comment on the initial guidance¹ for the Medicare Drug Price Negotiation Program as part of the Inflation Reduction Act (IRA).

ViiV, a global specialist HIV company established in 2009, is the only company solely dedicated to combating, preventing, and hopefully curing HIV and AIDS. ViiV specializes in the development of HIV medicines and is devoted exclusively to advancing science into HIV treatment, prevention, and care. From its inception, ViiV has had a singular focus to improve the health and quality of life of people impacted by this disease and has worked to address significant gaps and unmet needs in HIV care. ViiV is proud to be part of the scientific advances in the treatment and prevention of this disease, transforming HIV from a terminal illness to a manageable chronic condition.

An estimated 1.2 million people in the United States are living with HIV and there are approximately 38,000 new HIV diagnoses each year.² At least 13 percent are unaware they have the virus.³ Only 65 percent of diagnosed individuals had achieved viral suppression as of 2020, according to the CDC.⁴ Access to all modalities and new innovations for HIV treatment, and PrEP is an important consideration for the Medicare program and the populations it serves. Therefore, as the Centers for Medicare & Medicaid Services (CMS) implements the Medicare Drug Price Negotiation Program, we are concerned that CMS's policies will adversely impact meaningful innovation, create operational challenges, and limit

¹ [Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments \(cms.gov\)](https://www.cms.gov/medicare/coverage/coverage-determinations/initial-price-negotiation-program)

² Centers for Disease Control and Prevention (CDC). Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2019. HIV Surveillance Supplemental Report 2021;26(No. 2). <https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-vol-26-no-2.pdf>. Published May 2021. Accessed January 10, 2023.

³ HIV.gov. U.S. Statistics. October, 27 2022. <https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics>. Accessed January 10, 2023.

⁴ Centers for Disease Control and Prevention (CDC). Viral Suppression. September 2, 2022. <https://www.cdc.gov/hiv/statistics/overview/in-us/viral-suppression.html>. Accessed April 14, 2023.

patient access to transformative therapies. ViiV respectfully submits the comments below to highlight issues of interest to the patients we serve.

We make the following recommendations to CMS:

- I. HIV medications should be excluded from Medicare negotiation to ensure innovation continues for HIV treatment and prevention in order to:**
 - a. Support Ongoing Efforts to End the HIV Epidemic**
 - b. Align to CMS's Health Equity Goals**
- II. If HIV remains in scope for Medicare negotiation, we ask CMS to:**
 - a. Set the maximum fair price (MFP) at or near the manufacturer Wholesale Acquisition Cost (WAC) or list price.**
 - b. Expand Definition of Unmet Need to Include Public Health Considerations Like Adherence and Clinical Issues such as HIV Resistance**
 - c. Engage HIV Experts and Proactively Seek Broad Stakeholder Input**

Below are our recommendations with supporting rationales:

- I. HIV medications should be excluded from Medicare negotiation to ensure innovation continues for HIV treatment and prevention in order to:**
 - a. Support ongoing Efforts to End the HIV Epidemic**

As a public health issue, HIV is unique and advancements in treatment and prevention have the potential to eradicate the disease, but only if new options continue to be made available. CMS already treats HIV medications differently than other drug products in Medicare Part D. HIV is recognized as a one of only six “classes of clinical concern” or “protected classes” by Medicare due to the difficulty in managing the disease. Because of this HIV should be excluded from IRA’s MFP negotiation.

The Medicare Part D protected classes rule requires all (or substantially all) prescription drugs to be covered in six protected therapeutic classes including HIV.⁵ CMS adopted the Part D policy to “mitigate the risks and complications associated with an interruption of therapy for these vulnerable populations.”⁶ This protected class policy aligns with the recommendations of health experts, policymakers and HIV-specialized providers, who recommend unrestricted formularies in HIV treatment. The U.S. Department of Health and Human Services’ “Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV” emphasize the need for individualized treatment regimens to enhance adherence and ensure long-term treatment success.⁷ The same policy rationale should extend to ensure HIV treatments and preventions are protected in terms of setting MFP within this guidance.

⁵ CMS.gov. Medicare Advantage and Part D Drug Pricing Final Rule (CMS-4180-F). Jun 3, 2019. <https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-and-part-d-drug-pricing-final-rule-cms-4180-f#:~:text=Current%20Part%20D%20policy%20requires%20sponsors%20to%20include,antiretrovirals%3B%20and%206%29%20ant,ineoplastics%3B%20except%20in%20limited%20circumstances>. April 14, 2023.

⁶ CMS.gov. Medicare Prescription Drug Benefit Manual. Chapter 6 – Part D Drugs and Formulary Requirements. January 15, 2016. <https://www.cms.gov/medicare/prescription-drug-coverage/prescriptiondrugcovcontra/downloads/part-d-benefits-manual-chapter-6.pdf>. Accessed January 30, 2023.

⁷ Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. <https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new>. Accessed January 11, 2023.

HIV treatment and prevention options are public health tools that deserve unique considerations not similarly contemplated for other classes of biologics or drugs. Specifically, HIV treatment is beneficial to the patient, suppressing the virus, reducing complications and promoting the wellness of persons with HIV. In addition, once a person with HIV achieves viral suppression, HIV treatment also reduces the risk of sexual transmission of HIV to others.⁸ This “treatment as prevention” benefits population health. However, as mentioned previously, only 65 percent of diagnosed individuals had achieved viral suppression as of 2020, according to the CDC.⁹

The federal government has recognized public health benefits of treating HIV in its creation of the “Ending the HIV Epidemic Initiative: A Plan for America” (EHE),¹⁰ a bold national effort that aims to leverage scientific advances in HIV to end the HIV epidemic in the United States. The EHE focuses efforts across many federal health agencies, offices, and programs, including the US Department of Health and Human Services (DHHS) Office of the Assistant Secretary for Health, the Centers for Disease Control and Prevention (CDC), the Ryan White HIV/AIDS Program (RWHAP), the Health Resources and Services Administration (HRSA) Health Center Program, the National Institutes of Health (NIH), the Indian Health Service, and the Substance Abuse and Mental Health Services Administration (SAMHSA).¹¹ These federal agencies are working with state and local governments, health departments, and communities to develop jurisdictional plans to expand the use of the highest-impact HIV prevention strategies, including PrEP utilization.¹²

Additionally, in 2021, the White House and DHHS released the updated National HIV/AIDS Strategy (NHAS),¹³ which further outlines the federal commitment to ending HIV. The NHAS Federal Implementation Plan was released last year and outlines how the federal government will execute the national plan.¹⁴

This level of federal commitment to end a single disease is notable. ViiV urges CMS to consider how best to align the nation’s efforts to eradicate HIV with the goals of the IRA and its implementation, and respectfully ask that HIV products are excluded from negotiations.

b. Align to CMS’s Health Equity Goals

ViiV applauds the work of DHHS and CMS to promote health equity and to reduce racial and ethnic health disparities.^{15,16} The first pillar of the 2022 CMS Strategic Plan is advancing health equity, and the CMS Framework for Health Equity 2022-2032 prioritizes addressing the causes of health disparities

⁸ HIV.gov. Viral Suppression and Undetectable Viral Load. February 1, 2023. <https://www.hiv.gov/hiv-basics/staying-in-hiv-care/hiv-treatment/viral-suppression#:~:text=In%20addition%20to%20preventing%20sexual%20transmission%20of%20HIV%2C,transmission%20risk%20for%20people%20who%20inject%20drugs.%20>. Accessed April 14, 2023.

⁹ Centers for Disease Control and Prevention (CDC). Viral Suppression. September 2, 2022. <https://www.cdc.gov/hiv/statistics/overview/in-us/viral-suppression.html>. Accessed April 14, 2023.

¹⁰ HIV.gov. Ending the HIV Epidemic in the U.S. July 1, 2022. <https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview/>. Accessed April 14, 2023.

¹¹ HIV.gov. HHS Agencies Involved in Ending the HIV Epidemic. March 2, 2022. <https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/federal-action/agencies>. Accessed January 10, 2023.

¹² HIV.gov. HHS Agencies Involved in Ending the HIV Epidemic. March 2, 2022. <https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/federal-action/agencies>. Accessed January 10, 2023.

¹³ The White House. 2021. National HIV/AIDS Strategy for the United States 2022–2025. Washington, DC. <https://files.hiv.gov/s3fs-public/NHAS-2022-2025.pdf>. Accessed January 11, 2023.

¹⁴ National Strategy, Federal Implementation Plan for the United States | 2022—2025 https://files.hiv.gov/s3fs-public/2022-09/NHAS_Federal_Implementation_Plan.pdf. Accessed January 11, 2023.

¹⁵ Department of Health and Human Services. HHS Action Plan to Reduce Racial and Ethnic Health Disparities: A Nation Free of Disparities in Health and Health Care. Accessible at: https://www.minorityhealth.hhs.gov/assets/pdf/hhs/HHS_Plan_complete.pdf. Accessed February 07, 2023.

¹⁶ CMS.gov. CMS Framework for Health Equity 2022-2032. Accessible at: <https://www.cms.gov/files/document/cms-framework-health-equity.pdf>. Accessed February 07, 2023.

within CMS programs.^{17,18} Assuring equitable access to effective treatment for people with HIV and to optimal HIV prevention options for individuals who would benefit requires scientific innovation in HIV and drug options available to this vulnerable population.

Health disparities by race and ethnicity are particularly sobering for people with HIV. While 2019 HIV prevalence rates and new diagnoses among White and Hispanic/Latinx appear comparable at first glance,¹⁹ the burden of the disease comparatively across populations of color is much higher than White populations. The HIV epidemic continues to have a disproportionate impact on these communities, raising the risk of new infections with each sexual or injection drug use encounter.²⁰ In particular, Black/African American, and Hispanic/Latino communities are disproportionately affected by HIV compared to other racial/ethnic groups. For example, in 2019, the rate of new HIV diagnoses per 100,000 for Black people (45.0) was about 8 times that of white people (5.3); Latino people (21.5) had a rate 4 times that of white people.²¹ Similarly, Black women are disproportionately affected by HIV compared to women of other races and ethnicities. From 2014 to 2018, the rate of new HIV infections among Black women is 13 times that of white women and 4 times that of Latina women.²²

Black women are also disproportionately affected by HIV compared to women of other races and ethnicities. From 2015 to 2019, the rate of new HIV infections among Black women is eleven times that of white women and four times that of Latina women.²³ The clear racial disparities in HIV rates in the U.S. indicate a need for renewed focus on HIV prevention among people of color. Inequities in access to HIV prevention and treatment across populations most vulnerable have led to increasing racial disparities in HIV incidence, transmission, and viral suppression.²⁴

ViiV encourages CMS to align its efforts on IRA implementation to the agency's goals on advancing health equity and eliminating health disparities.

//. If HIV remains in scope for Medicare negotiation, we ask CMS to:

a) Set the maximum fair price (MFP) at or near the manufacturer Wholesale Acquisition Cost (WAC) or list price.

ViiV recommends CMS clarify that Wholesale Acquisition Costs (WAC) will be used as the basis to determine MFP discounts/rebates. CMS provides Primary Manufacturers the option to provide rebates “for the difference between the dispensing entity’s acquisition cost and the MFP.”²⁵ Manufacturers do not

¹⁷ CMS.gov. CMS Strategic Plan. February 03, 2023. Accessible at: <https://www.cms.gov/cms-strategic-plan>. Accessed February 07, 2023.

¹⁸ CMS.gov. CMS Framework for Health Equity 2022-2032. Accessible at: <https://www.cms.gov/files/document/cms-framework-health-equity.pdf>. Accessed February 07, 2023.

¹⁹ AIDS Vu, Local Data: United States, <https://aidsvu.org/local-data/united-states/>. Accessed January 11, 2023.

²⁰ Centers for Disease Control and Prevention (CDC). HIV by Group. April 14, 2022. <https://www.cdc.gov/hiv/group/raciaethnic/index.html>. Accessed January 11, 2023.

²¹ Kaiser Family Foundation (KFF). The HIV/AIDS Epidemic in the United States: The Basics. June 7, 2021. <https://www.kff.org/hiv/aids/fact-sheet/the-hiv-aids-epidemic-in-the-united-states-the-basics/#footnote-525108-42>. Accessed January 11, 2023.

²² U.S. Department of Health and Human Services. 2021. HIV National Strategic Plan for the United States: A Roadmap to End the Epidemic 2021–2025. Washington, DC. <https://files.hiv.gov/s3fs-public/HIV-National-Strategic-Plan-2021-2025.pdf>. Accessed August 29, 2022.

²³ The White House. 2021. National HIV/AIDS Strategy for the United States 2022–2025. Washington, DC. <https://files.hiv.gov/s3fs-public/NHAS-2022-2025.pdf>. Accessed January 11, 2023.

²⁴ Avalere.com. PACHA Highlights Need to Address HIV PrEP Coverage Disparities. April 07, 2021. <https://avalere.com/insights/pacha-highlights-need-to-address-hiv-prep-coverage-disparities>. Accessed February 07, 2023.

²⁵ CMS.gov. Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments. March 15, 2023. <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>. Accessed April 14, 2023.

normally sell direct to pharmacy locations. Instead, manufacturers sell products at WAC to wholesalers/distributors who then resell the product to pharmacy locations. A pharmacy's Actual Acquisition Cost (AAC) will likely not equal the cost for which the manufacturer sold the product. Use of AAC as the basis to determine MFP rebates may result in higher base prices than the list prices the manufacturer used for the sale of the drug. Manufacturers are not able to validate the AAC and varied cost bases will result in inconsistent MFP rebates paid for the same product to different pharmacies. AAC may include any third-party markups from entities in the supply chain that will inflate the price and result in higher rebates than required to effectuate the MFP. The use of WAC as the basis will ensure accurate effectuation of the MFP. WAC is a published list price set in advance and available to all entities in the supply chain.

b) Expand Definition of Unmet Need to Include Public Health Considerations Like Adherence and Clinical Issues such as HIV Resistance

CMS's proposed definition of unmet need in the guidance as "treating a disease or condition where very limited treatment options exist" is too limited when considering HIV.²⁶ We urge CMS to consider the public health ramifications of non-adherence in infectious diseases like HIV in defining unmet need. Within HIV there is a significant unmet need in terms of populations who have not been able to achieve adherence to their drug regimens (for either treatment or prevention). New scientific innovations that can address this need for adherence are, therefore, attempting to address this unmet need in a population. These non-adherent populations may be vulnerable, hard-to-reach, underserved populations with challenging social determinants of health, and necessitate different treatment options. The DHHS "Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV"²⁷ emphasize the need for individualized treatment regimens to enhance adherence and ensure long-term treatment success. Similarly, CDC's PrEP clinical guidelines also indicate that patient success in prevention benefits from availability of prevention options.²⁸

In addition, there is another unmet need in HIV treatment. Due to the fact that HIV virus constantly evolves and gain resistance to current treatments, the resistance landscape is constantly changing in HIV, and necessitates ongoing scientific research and innovation of new treatment options. In clinical settings, health care providers work closely with patients to select HIV treatment options with great specificity for each patient. Effective treatment of HIV is highly individualized and takes into account a patient's size, gender, treatment history, viral resistance, coexisting illnesses, drug interactions, immune status, side effects, and stigma. Specifically, viral resistance is a major factor that can limit drug efficacy, limit therapeutic options, and lead to cross-resistance to another drug.²⁹

c) Engage HIV Experts and Proactively Seek Broad Stakeholder Input

ViiV believes that experts, including scientists, manufacturers, advocates, patients, and clinicians, should be consulted when considering MFP. The voice and perspective of patients with lived experience in HIV have been a fundamental voice in the transformation of HIV from deadly virus to manageable chronic condition, to an epidemic that could be ended in our lifetime. Clinicians with disease-specific expertise

²⁶ [Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments \(cms.gov\)](#)

²⁷ Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. <https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines>. Accessed January 30, 2023.

²⁸ CDC. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States. 2021 Update Clinical Practice Guideline. <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf>. Accessed April 11, 2023.

²⁹ NIH. Drug Resistance. <https://hivinfo.nih.gov/understanding-hiv/fact-sheets/drug-resistance>. Accessed April 11, 2023.

and disease-specific clinical guidelines generated by clinicians should also play a meaningful role in CMS's determination of a selected drug's price.

Additionally, manufacturers are in a strong and unique position to inform CMS's value of a selected drug, based on extensive expertise and research on the benefits and impacts of their medicines throughout the product lifecycle. Thus, manufacturers should be able to share our expertise as a part of this process.

ViiV Healthcare appreciates the CMS's consideration of these comments on IRA and applauds the agency for its commitment to ensuring patients have equitable access to continued innovation. Please feel free to contact me at (770) 710-9620 or carie.a.harter@viiivhealthcare.com should you have any questions.

Sincerely,

A handwritten signature in black ink that reads "Carie Harter". The signature is written in a cursive, flowing style.

Carie Harter
Senior Director, Government Relations
ViiV Healthcare

April 14, 2023

Submitted via email to: IRAREbateandNegotiation@cms.hhs.gov

Dr. Meena Seshamani, M.D., PhD.
Department of Health and Human Services
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Medicare Drug Price Negotiation Program Guidance

Dear Dr. Seshamani:

Vizient, Inc. appreciates the opportunity to respond to the Centers for Medicare and Medicaid Services (CMS) Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (hereinafter the “Guidance”).¹ Also, Vizient thanks CMS for releasing additional resources to help stakeholders better understand the agency’s Inflation Reduction Act (IRA) implementation efforts and plans. The Guidance is for implementation of the Negotiation Program for initial price applicability year 2026. While Vizient is not commenting on all questions posed in the guidance, Vizient emphasizes the importance of considering healthcare providers’ perspectives as certain policies contemplated in the guidance may impact patient care.

Background

Vizient, Inc. provides solutions and services that improve the delivery of high-value care by aligning cost, quality, and market performance for more than 60% of the nation’s acute care providers, which includes 97% of the nation’s academic medical centers, and more than 20% of ambulatory providers. Vizient provides expertise, analytics, and advisory services, as well as a contract portfolio that represents more than \$130 billion in annual purchasing volume, to improve patient outcomes and lower costs. Headquartered in Irving, Texas, Vizient has offices throughout the United States.

Recommendations

Vizient appreciates the willingness of CMS to consider stakeholder feedback regarding Medicare drug price negotiation guidance issued on March 15, 2023. As noted in the Guidance, the IRA established the Medicare Drug Negotiation Program (hereinafter the

¹ <https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf>

“Negotiation Program”) to negotiate Maximum Fair Prices² (MFPs) for certain high expenditure, single source drugs and biological products. Vizient’s comments encourage CMS to clarify aspects of the Guidance and offers recommendations to improve transparency of the negotiation process.

Identification of Selected Drugs for Initial Price Applicability Year 2026

Identifying Potential Qualifying Single Source Drugs

In the Guidance, CMS indicates that the agency will identify single source drugs by using a process that applies to drug products and a separate process that applies to biological products. For biological products, CMS provides that “all dosage forms and strengths of the biological products with the same active ingredient and the same holder of the Biologics License Application (BLA), inclusive of products that are marketing pursuant to different BLAs.” As CMS is likely aware, biological products may have presentations in which there may be the same active ingredient/moiety but variation in administration, inactive ingredients or additional active ingredient/moiety (e.g., such as when a “biobetter” is developed³). Vizient encourages CMS to work with stakeholders to identify an evaluation process to determine when it would be appropriate group certain biological products together.

Delay in the Selection and Negotiation of Certain Biologics with High Likelihood of Biosimilar Market Entry

As noted in the Guidance, the Secretary may delay a biological from being selected for negotiation if certain circumstances are met, including if the Secretary determines there is a high likelihood that a biosimilar will be both FDA approved and marketed before September 1, 2025. Such a delay could occur if a Biosimilar Manufacturer’s Initial Delay Request⁴ is granted.

In the Guidance, CMS details that an Initial Delay Request must clearly demonstrate that patents related to the reference drug are unlikely to prevent the biosimilar from being marketed before September 1, 2025. CMS provides that it will consider this requirement met if “one or more court decisions establish the invalidity, unenforceability, or non-infringement of any potentially applicable non-expired patent relating to the Reference Drug that the patent holder asserted was applicable to the Biosimilar.”⁵ Vizient notes that there are often remaining, active patents for the reference product related to indications and that biosimilars will frequently enter the market with fewer indications than the reference product. As a result, market entry tends to

² As provided in the Guidance, “In accordance with section 1191(c)(3) of the Social Security Act, (“the Act”), maximum fair price means, with respect to a year during a price applicability period and with respect to a selected drug (as defined in section 1192(c) of the Act) with respect to such period, the price negotiated pursuant to section 1194 of the Act, and updated pursuant to section 1195(b) of the Act, as applicable, for such drug and year.”

³ See Sharma A, Kumar N, Kuppermann BD, Bandello F, Loewenstein A. Biologics, biosimilars, and biobetters: different terms or different drugs? *Eye (Lond)*. 2019 Jul;33(7):1032-1034. doi: 10.1038/s41433-019-0391-5. Epub 2019 Mar 7. PMID: 30846867; PMCID: PMC6707288, referring the term “biobetter” but noting that it has been widely used but is still not a defined term.

⁴ CMS will remove from the ranked list of 50 negotiation-eligible drugs as described in the Guidance any negotiation-eligible drug for which the inclusion on the selected drug list is delayed in accordance with the IRA. The IRA contemplates two potential requests under the Biosimilar Delay: (1) a request to delay the inclusion of a Reference Drug by one initial price applicability year (“Initial Delay Request”), as stated in the IRA; and (2) a request to delay the inclusion of a Reference Drug for which an Initial Delay Request has been granted for a second initial price applicability year (“Additional Delay Request”) as stated in the IRA.

⁵ Guidance, pg. 19

depend on whether there are substantive, non-expired patents. Vizient encourages CMS to clarify the Initial Delay Request policy in circumstances where a biosimilar may be marketed with fewer than all of the indications from the reference product.

Another circumstance that could be demonstrated in the Initial Delay Request related to whether the patent-related issues may prevent the biosimilar from being marketed is “the Biosimilar Manufacturer has a signed legal agreement with the Reference Manufacturer that permits the Biosimilar Manufacturer to market the Biosimilar in one or more dosage form(s), strength(s), and indication(s) before September 1, 2025, without imposing improper constraints on the Biosimilar Manufacturer.” Vizient appreciates the agency’s inclusion of this policy as it may encourage Reference Product manufacturers to make agreements with biosimilar manufacturers to support competition before the product would be potentially eligible for negotiation. Vizient encourages CMS to clarify “without imposing improper constraints on the Biosimilar Manufacturer”, as it is unclear how CMS will interpret this provision as different agreements develop, such as those that include licensing agreements.

Similarly, CMS indicates that it will consider active litigation to be determinative that there is not clear and convincing evidence that the biosimilar will be marketed before September 1, 2025. Vizient asks that CMS clarify whether the scope of the litigation will be considered, particularly where the biosimilar could be approved and marketed with a limited set of indications, even if there is ongoing active litigation.

Another requirement for the Initial Delay Request is that it must clearly demonstrate that the Biosimilar Manufacturer will be operationally ready to market the biosimilar before September 1, 2025. To assess this requirement, in part, CMS will consider “a manufacturing schedule consistent with the public-facing statements and any revenue expectations.” In addition, CMS includes in the process to submit an Initial Delay Request, that the biosimilar manufacturer include the manufacturing schedule for the biosimilar as submitted to the FDA during its review of the licensure application, to the extent available. Vizient encourages CMS to also consider collaborating with the Food and Drug Administration (FDA), to identify key milestones that would indicate the likelihood of approval and marketing and whether information could be more readily shared between FDA and CMS, especially if CMS would like to confirm aspects of the submission or if the agency has additional questions for FDA. Also, as FDA policy may evolve, we recommend CMS evaluate such policies for their impact on the negotiation process, including Initial Delay Requests.

Negotiation Factors

In the Guidance, CMS provides additional details regarding the sources CMS intends to use regarding therapeutic alternatives to a selected drug which would be relevant during the negotiation process.⁶ As provided in the Guidance, academic experts, clinicians and interested

⁶ As noted in the Guidance, “section 1194(e)(2) of the Act directs CMS to consider evidence about alternative treatments to the selected drug, as available, including:

parties may submit information on selected drugs and their therapeutic alternatives. While CMS notes that all such information related to drugs selected for initial price applicability year must be submitted to CMS by October 2, 2023, it is unclear how such information should be submitted, in what format and whether CMS will proactively identify data needs for interested parties' input. In addition, it is unclear whether CMS envisions a similar process for future price applicability years and whether such processes will be similar for Part B and Part D drugs.

Also, CMS indicates that it may consult outside subject matter and clinical experts on topics related to alternative treatments to the selected drug. Vizient actively provides data-driven insights to help healthcare providers achieve cost efficiencies, performance gains, and clinical improvements. For example, Vizient's [list](#) of essential medications for high-quality patient care is developed by Vizient pharmacy experts to identify medications where, if not available, would prove the greatest threat to a hospital's ability to provide immediate and high-quality patient care. The list also connects pharmacy leaders to mitigation strategies, which are ready-to-use documents with pertinent clinical and operational strategies to address shortages at the institutional level. Given Vizient's role in supporting members and pharmaceutical expertise, we would welcome any request from CMS to consult with our subject matter and clinical experts.

Lastly, as detailed in Appendix C of the Guidance, CMS indicates that 340B pricing data would be collected for use in the Negotiation Program. Vizient discourages CMS from using 340B pricing data for purposes of the Negotiation Program as doing so may have unintended consequences for the 340B Program. For example, Vizient is concerned that using 340B pricing to help set the MFP, which would be published, could result in commercial payers using this information to set discriminatory reimbursement for 340B covered entities based on that pricing. As a result, safety net providers would be limited in their ability to serve their communities. Also, Vizient notes that 340B prices are excluded from a manufacturer's non-federal average manufacturer price (non-FAMP) calculations. We encourage the agency to consider this information as it decides the appropriateness of collecting this information for negotiation purposes. While Vizient appreciates that CMS has provided some language in the Guidance to help ensure ongoing access to 340B pricing, we recommend CMS remove 340B pricing from the negotiation factors to help minimize disruption to safety net providers.

Establishment of a Single Proposed MFP for Negotiation Purposes

CMS indicates that, for the purposes of determining a single price included in an initial offer, the agency intends to base the single price on the cost of the selected drug per 30-day

1. The extent to which the selected drug represents a therapeutic advance compared to existing therapeutic alternatives for the selected drug and the costs of such existing therapeutic alternatives;
2. FDA-approved prescribing information for the selected drug and its therapeutic alternatives;
3. Comparative effectiveness of the selected drug and its therapeutic alternatives, including the effects of the selected drug and its therapeutic alternatives on specific populations (including individuals with disabilities, the elderly, the terminally ill, children, and other patient populations, herein referred to as "specific populations"); and
4. The extent to which the selected drug and the therapeutic alternatives to the drug address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy."

equivalent supply⁷, weighted across dosage forms and strengths, as applicable. Vizient suggests CMS consider price per 30-day treatment for oral medications and price per-dose for injectable medications. For injectable medications, this option may enable better comparisons between products that are listed as therapeutic alternatives.

In addition, Vizient encourages CMS to share information publicly regarding its application of this methodology, including its approach to identify a single price for use at each step in the negotiation process. While CMS notes that the Guidance is applicable to Part D drugs, such information may help inform stakeholder comments on future iterations of the Guidance and for Part B drugs. For example, additional information regarding circumstances where the single price was more challenging to calculate due to more complex dosing intervals would be helpful to share with stakeholders.

Also, as related to the methodology for developing an initial offer, CMS indicates that to evaluate the clinical benefit conferred by the selected drug compared to its therapeutic alternative(s), CMS aims to broadly evaluate the body of clinical evidence, including data received from the public and through consults with clinical and academic experts. As noted above, Vizient possesses a unique perspective, including data and analytics capabilities that would likely be relevant to the agency as it adjusts the starting point for the negotiation based on the clinical benefit. Vizient reiterates our willingness to serve as resource to CMS.

Per the IRA, CMS is to consider a range of factors when developing an initial offer, including manufacturer-specific data and evidence about therapeutic alternatives. In the Guidance, CMS also notes that in determining the initial offer, it will consider various aspects of a selected drug's clinical benefit drug compared to therapeutic alternatives. While not exhaustive, the agency indicates it will consider factors related to clinical benefit, safety and patient experience. Vizient encourages CMS to also consider resiliency and supply assurance when evaluating such products. While a more frequent concern with multisource medications, the market has had to withstand interruptions of sole source, branded pharmaceuticals, including biologic products.

Monitoring Access to the MFP

As provided in the IRA, the Primary Manufacturer⁸ is to provide access to the MFP to MFP-

⁷ CMS clarifies the cost of the selected drug would be per 30-day equivalent supply rather than per unit (e.g., tablet, capsule, injection)

⁸ As provided in the Guidance, "In section 1191(c)(1) of the Act, the Negotiation Program statute adopts the definition of "manufacturer" established in section 1847A(c)(6)(A) of the Act. Section 1193(a)(1) of the Act establishes that CMS will negotiate an MFP with "the manufacturer" of the selected drug. To the extent that more than one entity meets the statutory definition of manufacturer for a selected drug for purposes of initial price applicability year 2026, CMS intends to designate the entity that holds the NDA(s)/BLA(s) for the selected drug to be "the manufacturer" of the selected drug (hereinafter "Primary Manufacturer"). Likewise, for initial price applicability year 2026, CMS intends to refer to any other entity that meets the statutory definition of manufacturer for a drug product included in the selected drug and that either (1) is listed as a manufacturer in an NDA or BLA for the selected drug or (2) markets the selected drug pursuant to an agreement with the Primary Manufacturer as a "Secondary Manufacturer." Secondary Manufacturers would include any manufacturer of any authorized generics and any repacker or relabeler of the selected drug that meet these criteria."

eligible individuals⁹ at the pharmacy, mail order service or other dispenser at the point of sale, and to the pharmacy, mail order service, or other dispenser with respect to such MFP-eligible individuals who are dispensed the selected drug. Also, CMS “reiterates that the requirement to provide access to the MFP applies to all sales of the selected drug to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers that are providing a selected drug to an MFP-eligible individual”.¹⁰ Vizient appreciates the agency’s clarification as it may help prevent access challenges for providers. We encourage CMS to gain additional input from providers to determine whether other aspects of the Guidance should be clarified.

In the Guidance, regarding operationalizing access to the MFP, CMS also notes “there is widespread use of chargeback payments and rebate mechanisms among the pharmaceutical stakeholders in the private sector, which allows for entities to receive rebates or discounts on their purchases after those purchases are made, based on the specific population to whom the drug or biological is dispensed.”¹¹ Vizient is concerned that circumstances where the dispenser would have to submit for a rebate would add administrative burden, especially as additional review may be needed to identify when a rebate request would need to be submitted. Also, Vizient emphasizes the financial challenges that dispensers would endure due to higher inventory costs upfront and, adding to this, creating cash flow issues while waiting for both reimbursement and the manufacturer to make them whole. These financial challenges would be exacerbated as MFP reimbursement would also be lower. We encourage CMS to work with dispensers to identify options that would be less burdensome from both an administrative and financial perspective. Our comments would also apply should the agency consider a similar approach for Part B. We urge the agency to work closely with healthcare providers in refining this policy.

Similarly, we request the agency to work with providers in identifying their implementation needs and a process to report circumstances in which MFP pricing is not made accessible, including delays or burdensome processes to obtain such pricing. As noted, barriers to obtain such pricing could result in pharmacies and other dispensers taking financial losses that would likely be untenable and potentially jeopardize patient access to care. We urge CMS to carefully consider these concerns and regularly work with providers on solutions before and after implementation for both Part B and Part D. Further, we encourage CMS to develop policies to help ensure manufacturers provide prompt payment to providers and do not unnecessarily delay payments, including by imposing additional demands on providers.

⁹ As provided in the Guidance, “In accordance with section 1191(c)(2) of the Act, the term “maximum fair price eligible individual” means, with respect to a selected drug, the following: in the case such drug is dispensed to the individual at a pharmacy, by a mail order service, or by another dispenser, an individual who is enrolled in a prescription drug plan under Medicare Part D or an MA–PD plan under Medicare Part C (including enrollees in Employer Group Waiver Plans (EGWPs)) if coverage is provided under such plan for such selected drug; and/or in the case such drug is furnished or administered to the individual by a hospital, physician, or other provider of services or supplier, an individual who is enrolled under Medicare Part B, including an individual who is enrolled in an MA plan under Medicare Part C, if payment may be made under Part B for such selected drug.”

¹⁰ Guidance, p. 60

¹¹ Guidance, p. 65

Monitoring for Bona Fide Marketing of Generic or Biosimilar Product

As provided in the IRA, a selected drug will no longer be subject to the negotiation process if certain circumstances are met, including a determination that a generic or biosimilar has been marketed as evidenced by prescription drug event (PDE) data.¹² CMS intends to monitor whether “robust and meaningful” competition exists in the market once a selected drug is no longer a selected drug. While CMS seeks comment on the most effective ways to monitor whether robust and meaningful competition exists in the market, Vizient encourages the agency to first clarify what is meant by “robust and meaningful” competition.

Also, CMS provides examples of monitoring including whether the generic drug or biosimilar biological product is regularly and consistently available for purchase through the pharmaceutical supply chain, and whether it is available for purchase by community retail pharmacies in sufficient quantities from their wholesale suppliers. Vizient believes other data, such as national market share, presence at distributors, on group purchasing organization (GPO) contracts, and included in payer formularies could be among the several factors CMS considers to help inform whether “robust and meaningful” competition exists, depending on the context (e.g., Part B or D drugs) and product. Vizient also encourages CMS to gain insights from stakeholders as it evaluates whether “robust and meaningful” competition exists.

Research and Development Costs

In the Guidance, CMS outlines its interpretation of the primacy manufacturer’s research and development costs which are to be collected and used in the Negotiation Program. Vizient believes publicly sharing research and development costs, including recoupment of such costs, could help improve transparency. To the extent possible we encourage CMS to make this information publicly available. Should such availability not be possible, we suggest the agency consider making this information available in an aggregated view as this would also help improve transparency and understanding of true research and development expenditures.

Provider Input

Vizient understands that the IRA included several ambitious deadlines to which CMS has worked to adhere. We appreciate the agency’s efforts at promptly sharing information with stakeholders and seeking comment. As the agency continues to release guidance and resources regarding IRA implementation, we suggest the agency consider summarizing resources to better clarify the potential impact to providers and consistently seek their input. In addition, while the Guidance focuses on Part D drugs, we encourage the agency to clarify aspects of the Guidance that may also be applicable to Part B so that stakeholders may

¹² The two circumstances are, “(1) the FDA has approved a generic drug under section 505(j) of the FD&C Act that identifies as its reference listed drug a product that is included in the selected drug, or the FDA has licensed a biosimilar biological product under section 351(k) of the PHS Act that identifies as its reference product a product that is included in the selected drug; and, (2) the generic drug or biosimilar biological product, as applicable, is marketed pursuant to such approval or licensure.”

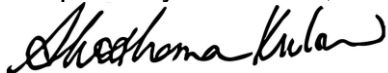
respond before the Part D policies are implemented and would potentially be more challenging to modify for Part B.

Conclusion

Vizient thanks CMS for the opportunity to share feedback in response to the Guidance. Vizient emphasizes the importance of minimizing provider burden and proactively engaging providers regarding IRA implementation plans to gain their feedback and perspectives.

Vizient membership includes a wide variety of hospitals ranging from independent, community-based hospitals to large, integrated health care systems that serve acute and non-acute care needs. Additionally, many are specialized, including academic medical centers and pediatric facilities. Individually, our members are integral partners in their local communities, and many are ranked among the nation's top health care providers. In closing, on behalf of Vizient, I would like to thank the CMS for providing us the opportunity to comment on the Guidance. Please feel free to contact me or Jenna Stern at jenna.stern@vizientinc.com, if you have any questions or if Vizient may provide any assistance as you consider these issues.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Shoshana Krilow".

Shoshana Krilow

Senior Vice President of Public Policy and Government Relations
Vizient, Inc.

