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AMERICA'S UNIONS

American Federation of Labor and Congress of Industrial Organizations

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April 14, 2023

Dr. Meena Seshamani, M.D., Ph.D.
Deputy Administrator and Director of the Center for Medicare
Center for Medicare & Medicaid Services
U.S. Department of Health & Human Services
200 Independence Ave., SW
Washington, DC 20201

RE: Medicare Drug Price Negotiation Program Guidance

Dear Deputy Administrator Seshamani:

The American Federation of Labor and Congress of Industrial Organizations (AFL-CIO) welcomes the opportunity to comment on the initial guidance covering the implementation of sections 11001 and 11002 of the Inflation Reduction Act. The AFL-CIO is a voluntary, democratic federation of 59 affiliated unions representing more than 12.5 million workers in all sectors of our economy. The AFL-CIO is committed to fairness in the workplace and health security for working people and their families. Our core mission is to ensure that working people are treated fairly and with respect, that our hard work is rewarded with family-supporting wages and benefits, and that our workplaces are safe. We also provide an independent voice in politics and legislation for working women and men and make their voices heard in corporate boardrooms and the financial system.

For over a century, labor unions have advocated for access to affordable and comprehensive coverage to make quality care available. While this country has made significant gains in coverage in recent years, for millions of working families, the high cost of care – particularly the high cost of prescription drugs – has created a significant financial barrier to necessary care. Nearly one out of three adults have skipped prescribed medicines due to costs – accounting for nearly half of all treatment failures and one-quarter of hospital and nursing home admissions. Even with good job-based coverage, union workers are adversely impacted by the rising cost of prescription drugs when year after year, they must pay higher and higher prices for the medications they need.

The situation in the U.S. is not one that workers in other industrialized countries face. Prescription drug prices are higher in the U.S. than elsewhere because our healthcare system allows drug companies to set prices. When fully implemented,

the Inflation Reduction Act (the IRA) will change that for the first time, and we are grateful for this Administration's commitment to passing this landmark legislation.

Relief from the high price of prescription drugs cannot come soon enough. For decades, drug companies have been largely unchecked in their ability to set the price of a drug based on what the market will bear. Over the years, the number of Medicare beneficiaries with high drug costs (defined as using the "catastrophic coverage cap") nearly tripled to 1.5 million annually between 2010 and 2019. During that decade, Medicare beneficiaries incurred $9.9 billion in out-of-pocket costs after the five percent copayments kicked in. This financial burden significantly impacts the household budgets of workers and retirees. Adults pay almost half — 48 percent — of their expenses for prescription drugs out-of-pocket, but persons aged 65 to 79 pay 56 percent, and those age 80 and older pay 67 percent of their total drug expenditures out-of-pocket.[1]

The AFL-CIO commends the Administration for providing such detailed guidance to stakeholders. We are grateful that CMS has provided stakeholders with this opportunity to comment, given that the IRA waives the notice and comment regulatory process required by the Administrative Procedures Act. Even though CMS could implement the law through program instruction and sub-regulatory guidance, it has allowed public input for the negotiation process as well as for other provisions of the IRA. Given the importance of this legislation and the gravity of the issue, we offer a few specific comments:

1. **Determination of a Negotiated Price**. 42 U.S.C. §1320f-3(b) requires CMS to develop and apply a consistent methodology and process for negotiating with drugmakers to arrive at an initial offer for each selected drug. According to the guidance, the agency will identify therapeutic alternatives for a drug and, based on the price of those therapeutic alternatives, develop an offer adjusted based on the clinical benefit of therapeutic alternatives. That preliminary offer will be further adjusted based on manufacturer-specific data, such as the amount of federal financial support for research and development (R&D).

   We are deeply concerned that CMS' proposed approach anchors the preliminary offer based on Part D net prices of therapeutic alternatives. As the guidance notes, the price of therapeutic alternatives may not reflect their clinical benefit, but the market power of the manufacturer based on exclusivity rights and anti-competitive practices and may be inflated compared to the price paid by other public payers as well as purchasers in the private sector and around the world. For instance, the Government Accountability Office found that Part D net prices were at least two to four times higher than publicly available prices in comparable countries in 2020. We agree with FamiliesUSA that relying on Part D prices would undermine the ability of the IRA to deliver significant cost savings for beneficiaries; using Part D prices would also ignore the often-hefty rebates that pharmacy benefit managers can negotiate – forgoing known savings available to other payers.

[1] *Data Profile on Prescription Drugs*, Georgetown Institute for Health Policy. Available at https://hpi.georgetown.edu/rxdrugs/#:~:text=Adults%20pay%20almost%20half%20%E2%80%94%2048,expenditures%20out%2Dof%2Dpocket.

CMS should consult with the Office of the Assistant Secretary for Planning and Evaluation and payers in the private sector to determine the most appropriate upper and lower bound price. As West Health has suggested, the Department should consider the list of factors in §1194(e)(1) could constitute the floor for price negotiations while the factors in §1194(e)(2) could constitute the ceiling, bearing in mind the statutory ceiling discussed in §1194(c).

Specifically, CMS should establish a price negotiation floor by identifying the marginal cost per unit of production of the drug and identifying any necessary premium required to recoup manufacturer research and development costs. The negotiated ceiling should be based on the incremental value of the therapy relative to other treatments, bearing in mind the cost-effectiveness of the treatment, as well as the manufacturer's return on invested capital over the remaining product life and the average return of other innovative sectors of the economy. The goal here is for CMS to 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.

Even with those factors, it is important to say that the maximum fair price CMS plans to offer should not be greater than the lowest price of a true therapeutic alternative that has demonstrated safety and efficacy matching that of the selected drug, including generic and biosimilar versions of therapeutic alternatives marketed in the U.S. A similar approach to internal, therapeutic reference pricing was incorporated into Denmark's pharmaceutical reimbursement in 2005.[2]

2. **Accuracy of a Drug Manufacturer Data**. As part of the drug negotiation process, CMS will request manufacturer-specific information on factors such as R&D costs, unit costs of production, federal financial support, and market data on sales and revenue in the U.S. CMS should rely on independent data sources whenever possible and consider contracting with private-sector firms to audit any manufacturer data that cannot be verified. It is critical that data relied on by CMS to estimate a maximum fair price to be accurate and complete.

3. **Specificity of Data Sought**. The cost of bringing innovative drugs to market is pivotal to determining the maximum fair price, and we agree with Public Citizen that HHS should not only require information on aggregate R&D but quite granular information that distinguishes between basic research, clinical research, the development of alternative delivery systems and dosages and other development activities. Moreover, each of those types of R&D expenditures should be disaggregated to allow HHS to risk-adjust R&D in

[2] Ulrich Kaiser, Susan J. Méndez, Thomas RØnde, Hannes Ullrich. "Regulation of Pharmaceutical Prices: Evidence from a Reference Price Reform in Denmark." February 2013. Available at https://docs.iza.org/dp7248.pdf. We recognize that transnational comparisons are difficult, and the Danish system is quite different. Denmark has a universal health care system and pharmacists are obligated to offer a patient the lowest price product within a group of substitutes unless it is barred by the prescription.

a more sophisticated manner. After all, the likelihood of clinical success and government approval varies significantly across different phases of the FDA approval process.

More granular data can also potentially enable the Department to prevent drug manufacturers from masking non-innovative R&D expenditures. As the House Oversight Committee discovered, a significant portion of R&D expenditures did not involve scientific work on innovative new drug therapies but instead focused on research intended to extend existing monopolies and suppress competition; firms would also include asset acquisition, such as the cost of purchasing a start-up that had developed a new drug where the price of the acquisition was based on expected revenue the new would generate, not the amount of money the target company spent on R&D.

4. **Release of Information**. Under §1193(c) of the statute, CMS may determine which information submitted by a drug manufacturer should be considered proprietary and protected by Exemption 4 of the Freedom of Information Act. We appreciate that the Administration must balance ensuring access to sensitive company information with keeping stakeholders fully informed. We urge the Administration to consider the impact of the passage of time and whether information that may have had commercial value during the FDA approval process remains commercially valuable many years later. With negotiations limited to single-source drugs that may have been approved more than a decade ago, this information may no longer be of commercial value. HHS should require manufacturers to demonstrate why information considered commercially valuable during the FDA approval process remains commercially valuable and deserving of FOIA protection.

5. **Agency Explanation**. Pursuant to §1195(a)(2) of the statute, CMS must publish an explanation for the maximum fair price by March 1, 2025. According to the guidance, the agency intends to make "high-level" comments about proprietary data. We urge the agency to reconsider how it handles specific categories of information, including marginal per unit cost of production, recouped and unrecouped R&D costs, and expected Medicare utilization over the remaining life of the product. We believe for these data elements that the agency should consider alternatives to the binary question of whether the Department release the specific number or not. The Department has an absolute obligation to explain the result of negotiations for a maximum fair price. We urge the Department to consider creative approaches that give a context for the data submitted by the manufacturer. For example, the Department could use metrics that provide a comparative or qualitative analysis of the data submitted. The Department could indicate:

    - the percentage of R&D costs that were recouped;
    - the percentage of Medicare utilization expected over the remaining product life;
    - the percentage of non-Medicare profits expected over the remaining product life; and

- the relative per unit marginal cost of production compared to other similar drugs (by decile).

A better understanding of this data, in addition to data on the cost of the drug overseas and the performance of this drug compared to therapeutic alternatives, could help the public understand the final negotiated price.

Conclusion

The IRA, if implemented correctly, could have a transformational impact on the affordability of care and the financial health of the Medicare program. We also hope that, given the size of the Medicare market for many pharmaceuticals, that these negotiations will temper prices in employer-sponsored insurance and other forms of coverage. We appreciate the opportunity to comment on this important guidance. If you have any questions, please feel free to contact me at lgoldberg@aflcio.org or (202) 637-5344.

Sincerely,

Lee Goldberg

Lee Goldberg, MA, JD

Arthritis Foundation®

April 14, 2023

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

RE: Medicare Drug Price Negotiation Program Guidance

Dear Administrator Brooks-LaSure:

On behalf of the nearly 60 million American adults and 300,000 children living with arthritis, the Arthritis Foundation appreciates the opportunity to comment on CMS' initial guidance for the Medicare Drug Price Negotiation Program for the implementation of the Inflation Reduction Act (IRA). Biologic medications are often used to treats autoimmune forms of arthritis like rheumatoid arthritis (RA), and we anticipate some of these would be included in the list of negotiated drugs. While the Arthritis Foundation does not take a position on the policy of Medicare drug negotiations, we are heavily involved in activities around cost-effectiveness and value assessment, two areas we know will be vital for determining methodologies for Maximum Fair Price (MFP).

The Arthritis Foundation has long advocated for a patient-centered approach to value assessment that incorporates and prioritizes patient preferences and quality-of-life goals. Our comments will expand on our engagement in and around value assessment and highlight our patient-centered value assessment principles, which we urge CMS to consider as it develops methodology for MFP.

AF Engagement in Value Assessment Activities

Multiple value assessments have been performed on rheumatoid arthritis (RA) drugs in recent years, prompting the Arthritis Foundation to publicly weigh in on the importance of patient engagement and patient data as a core component of the process and develop principles informed by our patient surveys, focus groups, expert interviews, and polls.

AF involvement in value assessment activities began in 2016 during a review of RA drugs by the Institute of Clinical and Economic Review (ICER). We have since engaged in a number of activities, including:

- A 2019 ICER re-review of RA drugs including biosimilars, in which we provided the patient perspective through public comments and during the expert panel and review meeting.

- Current participation in ICER's Fair Access Work Group, providing the patient perspective on ICER's fair access methodologies and reports.
- Current and past participation in National Health Council workgroups on Patient Core Outcomes Sets, utilizing our INSIGHTS assessment (Patient Reported Outcomes) as an example of collecting and utilizing patient outcomes data.
- Current participation in the Innovation and Value Initiative (IVI) Patient Advisory Council.
- Participation in health economic meetings including IVI's annual methods summit and the annual ISPOR meeting.
- Co-authorship with IVI on patient-centered methods in RA assessments, which included patient focus groups to guide contextual considerations in value assessments and led to a set of recommendations and best practices in patient-centered methodologies.
- Development of a patient coalition called Value in the States dedicated to driving meaningful patient engagement in value assessment-related activities.

Patient-Centered Value Assessment Principles

Increasingly, payers use value assessments to help determine coverage and formulary decisions. Patient experiences, preferences, goals, benefit-risk tolerance, and other factors must be incorporated into decisions, directly impacting patients' access to care. The patient experience must be considered holistically. Many people with arthritis have co-morbidities that impact their treatment choices and care. The lifetime considerations of health costs and outcomes cannot be measured in isolated episodes or short-term windows of time.

A good example comes from 2016 data as part of an RA drug review by the Institute for Clinical and Economic Review (ICER). Survey responses showed that patients on average had to try between 2 and 3 drugs before finding one that worked for their disease. Often patients found the drug to be less effective over time, prompting an additional round of treatment changes. Anecdotal evidence shed light on what happens when patients have disruptions in their treatment: symptoms often worsen, leading to the need for further intervention and treatment, and sometimes hospitalization. This data was critical to inform the ICER review process and led to recommendations in the final report about the inappropriate nature of step therapy in some cases.

In 2022 the Arthritis Foundation published a set of patient-centered value assessment principles we encourage CMS to consider in its continued development of IRA guidance. Relevant principles that CMS should consider in assessing value from this lens include:

1. Patient-Centered Methodologies.

The Arthritis Foundation appreciates CMS stating that it will not use metrics such as QALYs, and we recognize that the shortcomings inherent in how QALYs are often used. As such, we believe any survey tools should be patient-centered and fit-for-purpose such that policymakers assessing arthritis treatments can evaluate:

- Was the tool appropriate for arthritis?
- Did it have questions related to the disease?
- Did it consider validated joint-specific measurement tools?

Finally, as new methods evolve, value assessors should be transparent about the limitations of specific models. We encourage CMS to provide clear guidance on its plans to exclude QALY-based metrics from analysis. CMS should focus on additional methods when evaluating products, such as Multi Criteria Decision Analysis and Patient-Reported Outcomes registry data, and rheumatology-specific registries like the American College of Rheumatology's Rheumatology Informatics System for Effectiveness (RISE) Registry.

2. Real-World Evidence.

Clinical trial data is insufficient to capture the heterogeneity of disease, market access factors and other environmental factors crucial for understanding the impact of the treatment on the disease population.

Traditional value assessments cannot fully incorporate all necessary and relevant data to be truly patient centered until the treatment being assessed is on market. Should CMS include existing value assessments in its methodology, it should add cost and formulary data, patient-reported outcomes data and any other real-world data that would inform true cost-effectiveness.

3. Comprehensive Claims Data.

All payer claims databases (APCD) are large state databases that include information, such as medical claims and pharmacy claims collected from public and private payers. Robust APCDs can help inform value assessment analyses by providing data across sites of care and longitudinally about patients, allowing value assessors to identify trends and patterns in health care costs and better tailor coverage and cost decisions. We encourage CMS to utilize APCD data to help inform its MFP methodology.

4. Transparency.

Transparency across the health care ecosystem — from manufacturers to payers, pharmacy benefit managers and value assessors — is essential for implementing patient-centered value assessment. Currently, it is difficult to know the full set of processes and

factors that contribute to any given value assessment — and importantly how payers and other stakeholders are utilizing them.

CMS should be transparent about their methods and allow sufficient time for public input throughout the process and should establish a continuous feedback loop with the patient community to inform future post-value assessment decision making and any subsequent updates.

5. Meaningful Patient Engagement.

A truly patient-centered value assessment would engage patients in a meaningful way from start to finish and we urge CMS to consider the following principles for meaningful patient engagement as it develops and finalizes guidance and methodologies throughout the IRA implementation process:

- Patient engagement should never be considered a check-the-box activity. Instead, patients should be equal stakeholders throughout the process, and patient representatives should have voting privileges in any advisory councils or roundtables.
- Patient representatives should be invited to serve on Pharmacy and Therapeutic (P&T) Committees and other forums that determine formulary coverage decisions.
- Any advisory committee considering cost effectiveness should include robust patient representation, including voting membership and extensive quantitative and qualitative patient data.
- Patient representatives should be invited to craft value assessment methodologies and strategies, including legislative and regulatory processes and value assessment methodology design.

<u>Utilization Management Coverage Decisions</u>

We understand the negotiation process may alter market dynamics or shift incentives. This creates an important opportunity for CMS to ensure patient access to medicines and create appropriate guardrails, including limiting burdensome barriers such as prior authorization and step therapy.

Many utilization management protocols tend to apply step therapy policies that do not adequately align with clinical guidelines. The development of such protocols does not include patient input and the rationale, for such decisions is not typically publicly shared. Step therapy can lead to treatment delays and disease worsening when utilized inappropriately. This health insurance practice requires patients to try therapies preferred by the insurance company before approval for the therapy their doctor originally prescribed. When inappropriately used, step therapy can undermine the clinical judgment

of health care providers and put patients' health at unnecessary risk. Many patients must try multiple drugs before finding one that works for them, so the ability to remain on a drug that works is critical. An Arthritis Foundation survey found that >50% of all patients reported having to try 2+ drugs before getting the one their doctor prescribed.

We encourage CMS to more explicitly define coverage requirements to reduce the risk of plans denying coverage for products critical to patients. It is crucial that CMS continuously works to ensure access and remove barriers to both negotiated and non-negotiated drugs that providers and patients agree are necessary and appropriate. We encourage CMS to clearly disseminate a definition of coverage requirements and future guidance and/or future proposed coverage-related rules. CMS should work to keep patients in mind throughout the entirety of the process.

Timeframe Considerations

Understanding the need for a timely and swift process for the negotiation process, we strongly urge CMS to provide ample time for patients to share data and experiences pertaining to the negotiation processes. With a limited time of just 30 days to submit data after release of the list of drugs for negotiation, we are concerned this is insufficient time to submit data most beneficial to CMS, including research and data analysis. We request that CMS consider extending the timeframe for stakeholders to submit requested data or to allow for additional opportunities to submit information. The patient voice is critical during the negotiation process and must be included to create a more patient-centered approach.

Conclusion

As you consider methods to implement drug price negotiation within the Inflation Reduction Act, we welcome the opportunity to be a resource as staff or offer our patient experts to share perspectives in order to truly create a patient-centered implementation.

On behalf of the Arthritis Foundation, we thank CMS for the opportunity to provide input, and we look forward to collaborating with you to improve health care for patients living with chronic disease. Should you have any questions or if we can be of assistance, please contact Alisa Vidulich Casavant, Policy Director, at avcasavant@arthritis.org or Anna Hyde, VP of Advocacy and Access, at ahyde@arthritis.org or 202-843-0105.

Sincerely,

Anna Hyde

Anna Hyde
Vice President of Advocacy and Access
Arthritis Foundation

April 14, 2023

SUBMITTED ELECTRONICALLY

Centers for Medicare and Medicaid Services
Department of Health and Human Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

RE: Medicare Drug Price Negotiation Program Guidance

I. Introduction

The Biosimilars Forum is the independent trade association representing the biosimilars industry in the United States. The members of the Forum represent the companies with the largest portfolio of biosimilars in development today, as well as already on the market in the United States. Forum companies were the first to develop and launch biosimilars in the United States and continue to be those companies with the most experience in this industry. The Forum appreciates the opportunity to comment on the CMS guidance for the Biosimilars Special Rule Delay under the Inflation Reduction Act of 2022. The Forum also appreciates how open CMS has been over the past several months in listening to our concerns regarding the Biosimilars Special Rule Delay as drafted to date. As you will see from our comments, we continue to have grave concerns about the long-term impact of the Special Rule to the future of our industry as drafted.

Biologics play a critical role in the treatment of many serious illnesses, ranging from cancers to gastrointestinal diseases to genetic disorders. At the same time, although biologics represent only 2% of all U.S. prescriptions, they account for nearly 40% in net drug spending. *See* Biosimilars Forum, "Saving Billions on Healthcare Costs with Biosimilars," *available at* https://biosimilarsforum.org/wp-content/uploads/Biosimilars-Saving_Healthcare_Costs.pdf. The Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), Pub. L. 111-146 (Mar. 23, 2010), among other things, established section 351(k) of the Public Health Service Act ("PHS Act"), which provides an abbreviated licensure pathway for biosimilar and interchangeable biosimilar products.[1] While FDA only approved the first biosimilar fewer than ten years ago, these safe and effective medicines continue to generate substantial savings. Biosimilars cost about 30% less than the originator products they reference, and biosimilars have the potential to save $133 billion by 2025. *See id.*

On August 16, 2022, President Biden signed the Inflation Reduction Act ("IRA"), Pub. L. 117-169, into law. The IRA creates a price-setting framework for certain drugs and biologics (referred to as "selected drugs"). However, recognizing the importance of biosimilar competition to

[1] Unless indicated otherwise, the term "biosimilar" includes interchangeable biosimilars.

lowering healthcare costs and maintaining a robust marketplace, the IRA also includes the "Special Rule to Delay Selection and Negotiation of Biologics for Biosimilar Entry" (also referred to as the "Special Rule Delay"). *See generally* IRA § 11002. Under the Special Rule Delay, the Centers for Medicare and Medicaid Services ("CMS") must delay selection and negotiation of a biological product if there exists a "high likelihood" that a biosimilar referencing such product will be approved and marketed within a specified time period. *See* section 1192(f)(1)(A). The Special Rule Delay thus aims to maintain the incentives to invest significant resources in biosimilar development, against the negotiation framework introduced under the IRA.

CMS issued its "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 Guidance") on March 15, 2023. While we recognize the tight statutory deadlines under the IRA, the CMS Guidance improperly imposes substantive obligations without the required procedural safeguards of notice-and-comment rulemaking. Relatedly, stakeholders were deprived of the critical opportunity to comment on CMS's *ultra vires* statutory constructions and their real and detrimental consequences on the biosimilar industry and the competition it fosters. These procedural shortcomings are even more acute for Section 30 (including implementation of the Special Rule Delay), which CMS issued as final. The Forum may find that additional comments are necessary with respect to Section 30, and we note that without proper rulemaking, both the operations of Section 30 to impose obligations on Member Companies and any attempted enforcement thereunder are invalid. Nevertheless, given CMS's statement that it intends to issue revised guidance for initial price applicability year ("IPAY") 2026 and that it may make changes to any policies, including those on which it did not expressly solicit comment (CMS Guidance at 2), and because of the important impacts of Section 30 on other sections of the Guidance on which CMS *did* seek comment, the Forum is providing comment on the Special Rule Delay, including the portions described in Section 30.

In particular, the Forum is concerned that CMS's approach to the Special Rule Delay would exceed the statutory standard of a "*high likelihood*" of marketing by *September 1, 2025*, transforming it to a demonstration of *certain* marketing by *May 22, 2023*. This interpretation contravenes the statutory language and the established regulatory framework governing biosimilar development, approval, and marketing. Indeed, the regime constructed by CMS would effectively deny biosimilars the opportunity to avail themselves of the Special Rule Delay, frustrating Congress's objective in preserving this vital route for biosimilar competition. Moreover, CMS's Guidance, through its definition of "marketed" and its process for removing selected drugs from the list, would impose a new standard untethered from the IRA itself, which would further erode biosimilar competition by heightening the bar for delayed selection and removal of a reference product from the selected drug list. The CMS Guidance also leaves a number of critical questions unanswered. We are thus concerned that, without modification, the CMS Guidance will discourage biosimilar development and competition, and decrease patient access to affordable medicines, in direct contravention of the IRA's goals.

II. Background

Although section 351(k) of the PHS Act provides an abbreviated pathway for biosimilars, development remains time-consuming and expensive. The process begins with the foundation of biosimilarity, analytical similarity. The biosimilar manufacturer develops the product and its manufacturing process and undertakes critical comparative analytical testing with the reference product. Next, the biosimilar manufacturer designs and conducts clinical trials, including comparative pharmacokinetic studies and, oftentimes, comparative clinical safety and effectiveness studies. Throughout, the biosimilar manufacturer continues to generate analytical data and refines and scales up the manufacturing process. All-in-all, development generally takes between six and nine years and can exceed $150 million.

Throughout development, biosimilar manufacturers have the opportunity to engage with the Food and Drug Administration ("FDA" or the "Agency"). Typically, early in the development program, the biosimilar manufacturer has a Biosimilar Initial Advisory ("BIA") Meeting with FDA to solicit the Agency's feedback on the general feasibility of the program. The manufacturer may have one or more Biosimilar Development Program ("BPD") Type 2 meetings, which help resolve scientific questions and move the program forward; for example, FDA can provide input on the manufacturer's preliminary analytical data and whether such data is adequate to support proceeding with clinical trials. Prior to submission of the application, the biosimilar manufacturer has a BPD Type 4 meeting, at which point FDA and the prospective applicant come to consensus on the content and format of the application. FDA's engagement throughout the entirety of the development program—including at critical decision points—adds significant value and can increase the likelihood of an application's success.

Once development is complete, the biosimilar manufacturer submits a biologics license application ("BLA") to FDA (referred to as a "351(k) BLA"). FDA initially conducts a 60-day filing review to determine whether the application is sufficiently complete to permit substantive review. *See* Biosimilar Biological Product Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027 ("BsUFA III Commitment Letter"), *available at* https://www.fda.gov/media/152279/download. If filed, FDA intends to review and take action on the 351(k) BLA within 10 months of the filing date. *See id*. In other words, the review cycle totals one year from submission to FDA action. Similar to FDA engagement pre-submission, applicants also have opportunities to meet with FDA while the 351(k) BLA remains pending, including a Mid-Cycle Meeting and a Late-Cycle Meeting. These meetings provide applicants with status updates, including on significant issues identified during the review. *See id*. During the review cycle, FDA will conduct a facility inspection to ensure that it meets the standards designed to assure that the biosimilar continues to be safe, pure, and potent. 42 U.S.C. § 262(k)(2)(A)(i)(V); *see also* 21 §§ C.F.R. 600.21, 601.20(d). Once review is complete, FDA will either approve the 351(k) BLA or issue a Complete Response ("CR"), identifying the deficiencies that preclude approval. *See* 21 C.F.R. §§ 601.3, 601.4.

As a counterbalance to the expedited pathway for biosimilar competition, the BPCIA also provides periods of exclusivity for certain reference products (referred to as "reference product exclusivity" or "RPE"). Reference product exclusivity precludes the submission of a 351(k) BLA for four years (42 U.S.C. § 262(k)(7)(B)) and precludes FDA from approving such 351(k) BLA for 12 years (*id.* § 262(k)(7)(A)), both calculated from the reference product's date of first licensure. Accordingly, FDA cannot approve a 351(k) BLA referencing an RPE-eligible reference product until 12 years after the reference product's date of first licensure. For a reference product eligible for pediatric exclusivity, the foregoing time periods are extended to 4.5 years and 12.5 years, respectively. *Id.* § 262(m)(2)(A), (3)(A).

Separate from RPE, reference product sponsors can also obtain patents on their products, with patent life typically extending 14-20 years post-approval, or even longer. These patent portfolios include the "primary" patent (*i.e.*, that patent covering the compound, such as a monoclonal antibody) as well as "secondary" and "tertiary" patents (*e.g.*, those covering the original and subsequent indications and formulations as well as purity levels). Primary patents often expire after the 12-year RPE period—especially those that receive patent term extensions under 35 U.S.C. § 156 (which can extend a patent life for up to 14 years post-approval), with secondary and tertiary patents further prolonging patent protection.

Patent litigation cannot commence prior to the "artificial act" of infringement of 351(k) BLA submission. *See* 35 U.S.C. § 271(e)(2)(C). Once submitted, the biosimilar applicant and the reference product sponsor may engage in a series of information exchanges—informally known as the Patent Dance. *See* 42 U.S.C. § 262(*l*)(2)-(6). The Patent Dance, which typically takes upwards of 250 days, can whittle down the number of patents and culminates in the first wave of patent litigation. The biosimilar applicant precipitates the second wave of litigation with its notice of first commercial marketing, provided to the reference product sponsor at least 180 days prior to commercial marketing. *Id.* § 262(*l*)(8). A biosimilar applicant, however, need not engage in the Patent Dance, though it must still provide the reference product sponsor with the notice of first commercial marketing. *See Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664 (2017). Critically, unlike for generic drugs, initiation of patent litigation does not stay FDA approval of the pending 351(k) BLA. Accordingly, immediately upon approval and regardless of ongoing patent litigation, a biosimilar could seek to launch at risk.

III. CMS's Unattainable Interpretation of "High Likelihood" Exceeds its Statutory Authority

Under the process laid out in the Guidance, CMS is denying biosimilar applicants any process or opportunity for engagement prior to CMS's deadline for the Initial Delay Request, mere months before CMS publishes the selected drug list. But every biosimilar program is different, and "high likelihood" of approval and marketing cannot be determined in vacuum. Early engagement with CMS can provide critical information to help inform CMS's "high likelihood" determinations, if and when they are needed, and also ensure consistency with the FDA review and approval process.

a. High Likelihood of Approval

Under the IRA, a biosimilar may qualify for the Special Rule Delay if, among other things, there is a "high likelihood" of approval within two years of what would have been the selected drug publication date (September 1, 2025 for IPAY 2026). *See* section 1192(f)(1)(A). The CMS Guidance, however, limits eligibility only to those 351(k) BLAs approved or accepted for review by FDA on or before August 15, 2023. CMS Guidance at 19. This overly rigid position both contravenes the text and structure of the IRA and runs contrary to Congressional intent with respect to the Special Rule Delay.

To the extent that CMS believes its narrow definition of "high likelihood" of approval is tied to the language of section 1192(f)(3)(A), CMS is mistaken. *See id.* (referencing section 1192(f)(3)). That section provides that there *is* a "high likelihood" if CMS finds that "an application for licensure under section 351(k) of the Public Health Service Act for the biosimilar biological product has been accepted for review or approved" by FDA. The text does not say that there is *not* a high likelihood in other circumstances. To the contrary, the language describes one instance in which CMS *must* find a "high likelihood;" it protects biosimilar applicants from a different unduly narrow reading, under which CMS would theoretically have found "high likelihood" did not exist *even though* a 351(k) BLA had been accepted for filing or approved. This does not translate into an interpretation that precludes CMS from making such a "high likelihood" of approval finding in other scenarios.

The structure of section the IRA also makes clear the absurdity of this result. Given the one-year timeframe for FDA review of a 351(k) BLA, CMS's approach would truncate the requirement of "high likelihood" of approval within *two years* of the selected drug publication date to a timeframe of *ten months* after such date (the only window during which a biosimilar BLA *can* be either accepted for review or approved). In addition, given the 12-year RPE period, in certain circumstances, CMS's position would require a 351(k) BLA applicant to have submitted an application that FDA cannot approve in time to support a high likelihood determination under the CMS Guidance. To help illustrate, if a reference product, Reference Product A, were approved on January 15, 2016 and determined eligible for RPE, the 12-year period would expire on January 15, 2028. At the same time, Reference Product A would be eligible for selection on February 1, 2027, which would require a biosimilar applicant to submit a 351(k) BLA referencing Reference Product A no later than November 16, 2026 (*i.e.*, 60 days prior to January 15, 2027 to account for the filing review period). The assigned BsUFA date of November 16, 2027 would predate the RPE expiration date of January 15, 2028—or, for a reference product eligible for pediatric exclusivity, June 15, 2028. In other words, FDA could not approve the biosimilar within the timeline for review. Under CMS's interpretation, the biosimilar applicant would be left to choose between submitting an application that it knows is not approvable during the review cycle or forfeiting the

Special Rule Delay.[2] CMS's narrow reading thus cannot be reconciled with the IRA's structure. In short, the statute does not dictate—nor permit—CMS's interpretation.

b. High Likelihood of Marketing

The CMS Guidance states that a "high likelihood" of marketing requires, among other things, a demonstration that "the patents related to the Reference Drug are unlikely to prevent the Biosimilar from being marketed." CMS Guidance at 19. According to CMS, a biosimilar can only make this showing if it demonstrates one of the following with its Initial Delay Request (due no later than May 22, 2023):

> (1) there are non-expired approved patent applications[3] relating to the Reference Drug that are applicable to the Biosimilar; (2) 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; or (3) the Biosimilar Manufacturer has signed a 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.

Id.

Similar to "high likelihood" of marketing, CMS improperly concludes that it can *only* find a "high likelihood" of marketing if the conditions in section 1192(f)(3)(B) are met. Again, though, this provision only sets out when CMS is *required* to find a "high likelihood" of marketing, and CMS's determination that it is the *only* way to do so is extra-statutory. Moreover, in implementing its overly narrow interpretation, CMS provides three options, all of which effectively require complete patent clearance by May 22, 2023, discounting any and all activity that would occur over the next nearly 2.5 years. The IRA requires only a "high likelihood" of marketing by September 1, 2025. CMS's approach, however, further disregards the statutory language and completely reads out these two critical statutory elements, with CMS substituting its own standard of *certain* marketing by *May 22, 2023*, in disregard of its statutory mandate.

CMS's focus on patent clearance and its related conclusion that any ongoing patent litigation automatically disqualifies a biosimilar applicant from a special rule delay are both misplaced.[4]

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[2] Alternative benchmarks for "high likelihood" of marketing include, but are not limited to, information demonstrating that the biosimilar applicant had a BPD Type 4 meeting with FDA or completed any clinical trials in support of the anticipated 351(k) BLA.

[3] We assume CMS's reference to "approved patent applications" refers to issued patents. Patent applications are not enforceable. We refer to "patents" throughout under this foregoing assumption. For additional technical corrections, *see infra*, Section VI.

[4] *See* CMS Guidance at 20 ("CMS will consider active litigation to be determinative that there is not clear and convincing evidence that the Biosimilar will not be marketed before September 1, 2025, because litigation, including patent litigation, is historically unpredictable with respect to both the outcome of the litigation and the timing for resolution.").

There is always a risk that some patent exists that could conceivably cover the biosimilar. That does not mean, however, that such patents pose a risk to launch. Additionally, ongoing patent litigation does not automatically bar the marketing of a biosimilar. As noted above, patent litigation does not impact FDA approval of the pending 351(k) BLA, and a biosimilar can seek to launch at-risk at any point post-approval.[5] Indeed, a biosimilar manufacturer may have robust evidence that a patent is of low quality and plans to launch notwithstanding ongoing litigation. And, in some instances, ongoing patent litigation may even be irrelevant to biosimilar launch. As an example, assume Reference Product A is approved for rheumatoid arthritis and Crohn's Disease, and a biosimilar applicant initially seeks approval for both indications. Even if litigation remains ongoing for the patent covering the Crohn's Disease indication, the biosimilar applicant could amend or supplement its 351(k) BLA to "carve out" that indication from its labeling, launching the product for rheumatoid arthritis only.[6] Indeed, it is not uncommon for biosimilar applicants to add and remove indications as patent litigation evolves.

CMS's chosen criteria of the absence of unexpired patents or the resolution of all patent disputes thus fails to acknowledge that neither is a condition precedent for biosimilar marketing. Accordingly, they provide an overly restrictive barometer to demonstrate "high likelihood" of marketing. Moreover, as described in more detail below, all three criteria are effectively impossible to meet and would render the Special Rule Delay dead-on-arrival, in contravention of Congress's clear intent to preserve this avenue for biosimilar competition.

CMS's first criterion, that there are no, non-expired patents "relating" to the reference product and "applicable" to the biosimilar, fails to acknowledge the practices of reference product sponsors and realities of the patent system. The Special Rule Delay applies only to "extended monopoly drugs"—*i.e.*, those approved 12-16 years before any given IPAY.[7] Generally, patents expire 20 years after filing. *See* 35 U.S.C. § 154(a)(2). At the same time, reference products typically have extensive patent portfolios, that can include hundreds of patents. If just one of those patents were filed and issued after approval, a biosimilar could not satisfy this criterion. Meeting this threshold becomes even more strained when considering CMS's broad language of "related" to the reference product and "applicable" to the biosimilar. Such language could encompass patents on anything from a piece of equipment, a particular assay, or a spring used in an autoinjector. It is thus simply

[5] This stands in contrast to the patent resolution framework governing drugs regulated under the Federal Food, Drug, and Cosmetic Act ("FD&C Act"). There, initiation of timely patent litigation triggers a 30-month stay of FDA approval (21 U.S.C. § 355(c)(3)(C), (j)(5)(B)(iii)), precluding the possibility of launch until the stay expires or is otherwise extinguished.

[6] *See* CMS Guidance at 17 (noting that for CMS to grant an Initial Delay Request, the biosimilar need not include all of the reference product's indications); *see also* FDA Draft Guidance for Industry, *Biosimilars and Interchangeable Biosimilars: Licensure for Fewer Than All Conditions of Use for Which the Reference Product Has Been Licensed* (Feb. 2020) (explaining biosimilar applicants are not required to seek licensure for all of the reference product's conditions of use).

[7] As described by CMS, the Biosimilar Delay is applicable beginning IPAY 2026, notwithstanding the exclusionary language in section 1194(c)(4)(B)(ii) regarding extended monopoly drugs.

not feasible that all such patents would have expired within 16 years post-approval of the reference product.[8]

Biosimilar applicants are thus left 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. At the outset, this would disqualify any 351(k) BLAs submitted after May 22, 2023 from eligibility, as patent litigation cannot commence until after application submission. *See id*. § 271(e)(2)(C). And, any expectation that reference product sponsors and biosimilar applicants should come to an agreement, consistent with the third criterion, *before* submission of an application is not reasonable. It would obligate a biosimilar manufacturer to disclose its confidential development plans to its competitor. *Cf*. 21 C.F.R.§ 601.51 (recognizing the existence of a pending 351(k) BLA as confidential commercial information). It would also undermine the Court's conclusion in *Sandoz* that a biosimilar applicant is not required to notify a reference product sponsor of the existence of its application nor provide confidential access to such application. *See* 137 S. Ct. at 1675-76. Ultimately, this outcome of excluding all 351(k) BLAs submitted after May 22, 2023 from the Special Rule Delay contravenes the statutory language and even CMS's own recognition that a biosimilar application accepted for review by August 15, 2023—and thus submitted by June 16, 2023—may be eligible for a Special Rule Delay. *See* CMS Guidance at 19.

Applications submitted by May 22, 2023 do not fare much better, as CMS's requirements do not appropriately consider the practicalities of patent litigation and the statutory requirements governing these disputes. 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 submitted its 351(k) BLA by September 14, 2022. For a court decision by the May 22, 2023 date, however, a three- to four-year litigation period would necessitate 351(k) BLA submission by September 2019, at the latest.[9] Expecting a biosimilar to have somehow predicted the IRA and submitted its 351(k) BLA in this timeframe is unreasonable—even more so because many reference products eligible for delayed selection remain protected by reference product exclusivity well-past September 2019 and September 2020, the date on which FDA would take action on the pending 351(k) BLA. In other words, CMS would have a biosimilar manufacturer not only anticipate the enactment of the IRA but also structure its development program to facilitate submission of a 351(k) BLA that may not have been even eligible for approval given blocking reference product exclusivity. Foregoing the Patent Dance, and shaving off 250 days, would make little difference; also, nothing in IRA suggests that

[8] For clarity, we assume that a biosimilar manufacturer could satisfy this criterion by demonstrating that there were no applicable patents to a single strength and dosage form under development (as opposed to all strengths and dosage forms under development). Nevertheless, for the reasons described, this slight narrowing of scope would not result in a different outcome.

[9] We assume that "court decision" in the CMS Guidance refers to a district court decision and not a decision from which no appeal can be taken (other than a petition to the United States Supreme Court for a *writ of certiorari*). Should CMS mean the latter, it would serve only to necessitate even earlier submission of a 351(k) BLA.

the legislation was intended to alter the provisions governing the Patent Dance or a biosimilar manufacturer's calculation of whether to engage in it.

Even reaching a settlement agreement by May 22, 2023, would be a tall order. While a settlement may occur earlier than a court decision, initiating litigation and arriving at a settlement still take time. This is particularly true for first-to-market biosimilars, with biosimilar manufacturers gaining more settlement leverage as litigation proceeds and additional information is gleaned to expose the asserted patents' low quality or likely invalidity. Again, though, this assessment requires time, rendering CMS's selected May 22, 2023 cutoff virtually impossible to meet.

We appreciate CMS's objective of identifying benchmark events to inform the "high likelihood" of marketing determination, but the ones CMS chose both fail to comport with the statute and would effectively deprive any biosimilar manufacturer from availing itself of the Special Rule Delay. Preserving the functionality of the Special Rule Delay and giving credence to Congress's clear intention to preserve the incentives for biosimilar development thus requires expanding the criteria to include those that account for the existing patent resolution framework and provide adequate flexibility to reflect the varying circumstances of each biosimilar applicant. Accordingly, we respectfully request that CMS conclude that each of the following individually would suffice to demonstrate a "high likelihood" of marketing by September 1, 2025 (whether such information is included in the Initial Delay Request or in an update provided by August 15, 2023):

- A copy of a notice of first commercial marketing pursuant to 42 U.S.C. § 262(*l*)(8), which the biosimilar applicant must provide to the reference product sponsor no later than 180 days before the date of first commercial marketing;
- An attestation that, for any ongoing patent litigation, the court has issued neither a preliminary injunction nor a permanent injunction preventing launch by September 1, 2025;
- Public statements from the biosimilar manufacturer that it is planning for biosimilar launch before September 1, 2025 (*e.g.*, press statements, excerpts from investor relations reports or meetings, and public statements from a corporate director). These statements could also be accompanied by an attestation signed by the General Counsel and/or Chief Executive Officer. The fiduciary obligations biosimilar companies owe to their shareholders ensure accountability, providing a preexisting check against self-serving statements;
- Public statements from the reference product sponsor that it is planning for biosimilar launch before September 1, 2025 (*e.g.*, in disclosures to the United States Securities and Exchange Commission);
- Biosimilar market entry forecast by an industry-leading analytics firm, such as IPD Analytics. These firms prepare data-driven forecasts of anticipated market entry based on tracking litigation and mapping out the patent landscape;

- An executive summary of a law firm's assessment of the asserted patents' invalidity and non-infringement.

Each of these additional criteria provides clear and convincing evidence that the biosimilar will be marketed by September 1, 2025, thus demonstrating a "high likelihood" of marketing by that date. They may not provide the certainty CMS is looking for, but certainty is beyond the bounds of what the IRA requires.

IV. CMS's Interpretation of "Marketed" Exceeds Its Statutory Authority and Erects Unnecessary Barriers to Biosimilar Competition

A number of IRA provisions are conditioned on when a biosimilar is "marketed," including the Special Rule Delay (*see generally* section 1192(f)), whether or not a "drug product" continues to be a "qualifying single source drug" ("QSSD") (section 1192(e)(2)(B)(iii)), whether a selected drug will continue to be negotiation eligible (section 1192(c)(2)), and whether a selected drug will remain a selected drug (section 1192(c)(1)).[10] *See, e.g.*, CMS Guidance §§ 30, 70, 90.4. Without caveat or limitations, each of these provisions in the IRA refers to whether the biosimilar is "marketed" in the sense that "marketed" has been clearly defined by the Department of Health and Human Services. *See, e.g.*, Medicaid Drug Rebate Data Guide for Labelers § 4.15; 21 C.F.R. § 314.3.

Perhaps in recognition of this unambiguous and established meaning of the term "marketed," the CMS Guidance states that "marketing" is defined as "the introduction or delivery for introduction into interstate commerce." CMS Guidance, Appendix C. Despite this acknowledgement, CMS goes on to create a separate, *ultra vires* definition of "marketed," which inexplicably requires that the marketing must be "*bona fide*"—meaning, potentially, that it must be sold in "sufficient quantities" or meet some threshold of "market share." CMS further adds the requirement that "*bona fide*" marketing can only be demonstrated with prescription drug event ("PDE") data. This interpretation plainly exceeds CMS's statutory authority and creates unnecessary and ungrounded hurdles to biosimilar competition.

Further, the PHS Act includes repeated references to "commercial marketing." It serves as one of the triggers for first interchangeable exclusivity (*see* 42 U.S.C. § 262(k)(6)(A)) and also precipitates the notice of commercial marketing (*see id*. § 262(k)(8)). While FDA has not yet explicitly defined these terms in the context of the PHS Act, it has done so for abbreviated new drug applications ("ANDAs"), with FDA's duly promulgated regulations providing that "commercial marketing" means the introduction or delivery for introduction into interstate commerce of the drug product. *See* 21 C.F.R. § 314.3. CMS gives no justification for departing from this well-established meaning. Moreover, in all likelihood, given CMS's approach here, a biosimilar application would have two, inconsistent dates on which it is considered marketed: one

[10] *See* Section V, *infra*, for comments on CMS's interpretation of section 1192(c) and its determination that the MFP will apply for IPAY 2026 if a biosimilar launches after the negotiation period but before January 1, 2026.

for purposes of first interchangeable exclusivity and for the notice of first commercial marketing under the PHS Act, and another for "marketing" under the IRA.

a. The Requirement for "*Bona fide*" Marketing Will Hinder Biosimilar Development

As mentioned, CMS's requirement of "*bona fide*" marketing lacks grounding in the statute. Equally as problematic, and equally as divorced from its statutory authority, CMS imbues this extra-statutory requirement with the vague standard of "robust and meaningful competition" as evidenced by some yet-to-be-defined thresholds for available sufficient quantities and market share. *See* CMS Guidance at 67. Through the requirement for "*bona fide*" marketing, CMS grants itself the discretion to negotiate a drug *even after a biosimilar has been marketed*, in direct contravention of the IRA. But CMS was not granted that authority by Congress, and it cannot legislate on its own behalf.

These interpretive infirmities have significant consequences. Notwithstanding the *actual* date of marketing for a biosimilar, it could take weeks, months, or even longer before the biosimilar passes CMS's arbitrary threshold of "*bona fide*" marketing. CMS, however, fails to consider that often, factors outside the biosimilar manufacturer's control can drive uptake. Myriad factors, from supply disruptions to physician education can impact the pace at which biosimilar uptake happens. Additionally, although equally safe and effective, only biosimilars FDA has determined to be interchangeable may be substituted for their reference products. *See* 42 U.S.C. § 262(i)(3). Building market share thus can take time, a process further complicated by rampant misinformation about biosimilars and rebate traps that frustrate biosimilar market share regardless of launch efforts.

The artificial delay created by CMS could thus culminate in price negotiation of a reference process *regardless* of biosimilar competition, and the time and resources it took to launch that biosimilar. Other examples of the adverse impacts of "*bona fide*" marketing abound, such as the impermissible narrowing of the one-year marketing delay exclusion from the Special Rule Delay (*see* section 1192(f)(2)(D)(iii).[11] The *ultra vires* "*bona fide*" marketing requirement becomes even more problematic when combined with CMS's approach to defining a "selected drug." Because CMS is considering all dosage forms and strengths of a biological product with the same active ingredient that share a BLA holder to be a single "drug" for purposes of negotiating (*see* CMS Guidance at 8), a "selected drug" may consist of a dozen or more products, with different indications and presentations. A biosimilar applicant might target one, or a single product, with a single biosimilar—exclusivity might even block some or most of the reference product's unique products—or it might target several. *See* CMS Guidance at 17 (eligibility for the Special Rule Delay does not require a biosimilar applicant to seek licensure of all the dosage forms, strengths, and indications of the reference product). This is a complicated, multi-faceted decision. Expecting a biosimilar manufacturer to reach the same threshold in both circumstances makes little practical

[11] *See also infra*, Section V.

sense. On the other hand, adjusting the so-called marketing threshold for different products would underscore the subjectivity and arbitrariness of the "*bona fide*" marketing requirement and exacerbate the uncertainties in an already increasingly unpredictable process.

A biosimilar manufacturer is already racing against the clock to meet the IRA's deadlines. CMS's extra-statutory requirement that marketing must be "*bona fide*" would truncate these timelines. Moreover, biosimilar manufacturers will lack any certainty as to when, or even whether, they could meet this subjective standard, particularly given the role of external factors. The absence of a predictable and stable process, combined with the seeming inevitability of negotiation, will broadly chill biosimilar development and its promise of increased access and lower drug prices.

b. PDE Data Are Not a Suitable Proxy for Marketing

CMS's plan to use PDE data as a proxy for marketing similarly raises concerns. At the outset, CMS only plans to consider PDE data from August 16, 2022 through August 16, 2023 in its evaluation of whether a drug meets the QSSD criteria. *See* CMS Guidance at 10. Nowhere in the statute, however, does it require that the biosimilar have been marketed *only* in the past year. And, there are numerous reasons why there may be a gap in marketing, particularly given supply challenges precipitated by the COVID-19 pandemic.

PDE data is also both too narrow in scope and insufficiently time-sensitive to determine whether and when a biosimilar is marketed. Marketing means *any* introduction or delivery for introduction into interstate commerce. The statute contains no restriction on to *whom* the biosimilar is marketed. CMS's use of PDE data, with its limitation to Medicare Part D beneficiaries, however, does just that. *See* Questions and Answers on Obtaining Prescription Drug Event (PDE) Data, *available at* https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/Downloads/PartDClaimsDataQA.pdf (explaining that PDE records are not available for Medicare beneficiaries who are not enrolled in a Part D plan). Moreover, the use of PDE data implies formulary access, but such access can take months to account for the formulary submission, review, and approval process. Relatedly, mid-year formulary changes for biosimilars are often tied to a certain date and require review by pharmacy-and-therapeutics committees and CMS. The latter review can delay actual formulary coverage and access given CMS's prevailing view that replacement of originators with biosimilars constitutes a negative/non-maintenance change. PDE data also lacks real-time reporting, with sponsors submitting data only at the first quarter and monthly thereafter. With the precise date of marketing carrying such significant weight, any time lag could have devastating consequences to a biosimilar.

The use of PDE data to measure biosimilar marketing also further exacerbates CMS's groundless requirement of "*bona fide*" marketing, as PDE data typically skews in favor of the reference product—an outcome partly tied to CMS's own policies. For example, long-standing branded rebate agreements (volume contracts) with Pharmacy Benefit Managers ("PBMs") can frustrate biosimilar marketing, regardless of the manufacturer's efforts and resources. And, CMS's own policies allow PBMs to extract bigger rebates from originator biologics by the mere threat of biosimilar competition, while causing little list price erosion. Given the persistence of anti-

competitive rebate contracts that give maximum power to high-cost, originator biologics, by both requiring "*bona fide*" marking and a demonstration of such marketing based on PDE data alone, CMS improperly stacks the deck against biosimilar competition.

CMS's approach thus fails to give the statutory term "marketed" its appropriate breadth and implausibly cuts off avenues for price competition through biosimilar entry. Only real-time, comprehensive marketing information would suffice to determine whether a biosimilar is approved and marketed. If, however, CMS determines that claims data is necessary, notwithstanding the absence of any statutory requirement stating so, it should assess raw data or data made available through a transaction facilitator, which would at least provide information that more closely resembles real-time data and the entire market.[12]

Otherwise, we respectfully request that CMS should only conclude that an approved biosimilar is *not* marketed in consultation with FDA, based on a determination that the biosimilar applicant provided notice under 21 U.S.C. § 356i(b) (*i.e.*, that the biosimilar will not be available for sale), and the biosimilar applicant has not subsequently informed FDA that the biosimilar should no longer be listed as discontinued in the Purple Book.

V. CMS's Procedure for Removing Drugs from the Selected Drugs List Is Not Authorized by Statute and Will Chill Biosimilar Development

According to CMS, if a biosimilar is approved and marketed during the negotiation period, the maximum fair price ("MFP") will not apply for IPAY 2026, but, if the biosimilar reaches the market a day later, but still well before IPAY 2026, the MFP will nevertheless apply for IPAY 2026. *See* CMS Guidance at 62-63. This approach, which effectively freezes a drug's QSSD status as of August 2, 2024 and imposes substantial consequences depending on a day difference of biosimilar launch, exceeds CMS's statutory authority. The IRA plainly states that IPAY 2026 begins on January 1, 2026, but CMS instead would have it effectively begin on August 2, 2024. Nowhere does the IRA authorize—or even suggest—that CMS can impose a MFP on a biological product that does not meet the QSSD definition. To the contrary, the statute expressly ties the QSSD definition to the initial price applicability year. *See* section 1192(e)(1); *see also* section 1191(b)(2). We note that the Guidance's reference to section 1192(c) cannot salvage this interpretation. Section 1192(c)(1) describes the circumstances during which a selected drug will (or will not) remain a selected drug. Section 1192(c)(2), itself billed as a "clarification," merely conveys additional circumstances during which a selected drug will remain a selected drug. CMS, however, would have this "clarification" impose draconian consequences on selected drugs with biosimilar competitors that launch well-before January 1, 2026 but after the close of negotiation—an unsupportable reading of the text.

Beyond its statutory failings, CMS's approach also stymies biosimilar competition. The 11-year grace period before drug selection offers little relief for biosimilars, as a biosimilar cannot be

[12] CMS recently adopted a similar approach in the context of COVID-19 vaccine data. *See* CMS Memorandum, Access to COVID-19 Vaccine Data for Parts C & D Enrollees (Jan. 7, 2021).

approved, let alone marketed, for *12 years* after approval of a RPE-eligible reference product. Indeed, a reference product approved on August 16, 2012 would be eligible for drug selection for IPAY 2026 but, given the 12-year RPE period, a biosimilar could not even be approved by CMS's arbitrary August 2, 2024 date. Given the potential for pediatric exclusivity to extend the 12-year RPE period by six months, the same outcome could arise from reference products approved as early as February 2, 2012. Moreover, while the Special Rule Delay provides some respite, its stringent statutory eligibility requirements are challenging to meet.

Under the IRA, *only* QSSDs are subject to price controls. Depriving biosimilars of this critical additional time to secure approval and launch will result in delayed price decreases and decreased competition. Biosimilar entry during this period would facilitate price erosion prior to MFP, ensuring patients have access to less expensive, safe and effective medicines sooner. More broadly, collapsing the minimum statutorily provided period before applicability of the MFP from 13 years post-approval to just over 11 years, will significantly deter biosimilar development, with manufacturers unable to justify the high costs in the face of almost certain negotiation.

VI. Technical Corrections and Need for Additional Information

In addition to the overarching comments above, the Forum also proposes technical corrections for CMS's consideration. In addition, we include several areas where additional information is necessary in order for developers to have the predictability and stability necessary to support continued investment in biosimilars.

a. Clarify that 351(k) BLAs in Complete Response ("CR") Status Are Eligible for the Special Rule Delay

At the end of the one-year review cycle for a BLA, FDA generally either approves the 351(k) BLA or issues a CR Letter identifying the deficiencies that preclude approval. If a biosimilar applicant receives a CR Letter, the applicant generally will work to address the deficiencies and resubmit the 351(k) BLA. FDA will generally act on a resubmitted 351(k) BLAs within six months of receipt. *See* BsUFA III Commitment Letter.

The Forum respectfully urges CMS to revise the Guidance and make clear that a 351(k) BLA in CR status remains eligible for the Special Rule Delay, as it would still be considered accepted for review by August 15, 2023, consistent with the CMS Guidance. *See* CMS Guidance at 19. We note that the six-month period for FDA review provides ample time for approval by September 1, 2025.

b. CMS Should Provide Further Clarity Regarding What "Publicly Available Data" It Will Consult to Determine the Likelihood their Reference Product Will be a Selected Drug

According to the Guidance, CMS does not intend to provide any advance notice of or seek any public input on a drug's QSSD or negotiation-eligible status in advance of September 1, 2023 selected drug publication date. At the same time, preparing an Initial Delay Request will require

time and resources. While we appreciate CMS's advice to consult "publicly available information" to inform biosimilar manufacturers' assessments of any given reference product's likelihood of selection, the CMS Guidance is conspicuously silent on the identity of such information. *See* CMS Guidance at 21 n.19.

To the extent CMS expects biosimilars to rely on available Medicare Part D statistics, such information remains woefully outdated. Indeed, as of April 13, 2023, the latest data available was from 2021. *See* CMS, CMS Program Statistics – Medicare Part D, available at https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-service-type-reports/cms-program-statistics-medicare-part-d. Moreover, expenditure information is necessary, but not sufficient, to evaluate the potential for selection. Without further clarity, biosimilar manufacturers will be left in the difficult position of preparing Initial Delay Requests for all of their reference products or risk forfeiting a Special Rule Delay and having their biosimilar development programs undermined by assignation of an MFP to the reference product. To help fill this gap, CMS should publish its list of negotiation-eligible drugs in advance of the due date for the Initial Delay Request. Additionally, CMS could set up a process for biosimilar manufacturers to obtain CMS's views on whether it considers a particular reference product to meet the definition of QSSD. At minimum, CMS should identify the sources it intends to use and make such information public.

c. CMS's Requirements Should Reflect an Accurate Understanding of Biosimilar "Manufacturing Schedules"

Pursuant to the PHS Act and FDA's implementing regulations, a proposed biological product must be "available for inspection" during the pendency of the 351(k) BLA. *See* 21 C.F.R. § 601.20(d); *see also id*. § 600.21; 42 U.S.C. § 262(k)(2)(A)(i)(V), (k)(3)(B). Accordingly, the establishment that will manufacture the biological product must be in operation and manufacturing the proposed product at the time of application submission, and FDA will only approve the application after inspection of the facility. *See id.* To facilitate this pre-approval inspection, FDA expects that each 351(k) BLA contain a manufacturing schedule. The manufacturing schedule submitted to FDA—and thus the one submitted to CMS under section 1192(f)(1)(B)(ii)(III)(aa)—does not reflect any post-approval manufacturing dates, let alone a schedule "consistent with public-facing statements and any revenue expectations." CMS Guidance at 20.

While the manufacturing schedule only includes pre-approval dates, it still suffices to alleviate CMS's concerns about operational readiness. *See id*. at 19-20. Indeed, the manufacturing schedule signals to FDA that the establishment is prepared and able to manufacture the proposed commercial product during the application review. Accordingly, no additional manufacturing information is needed, and we respectfully request that CMS revise the Guidance to omit the reference to "consistent with the public-facing statements and any revenue expectations."

d. Licensure Status in the Initial Delay Request Form Requires Further Clarification

As described in the CMS Guidance, a biosimilar may qualify for the Special Rule Delay presuming its 351(k) BLA is accepted for filing by August 15, 2023. *See* CMS Guidance at 19. Given the 60-day filing review, the 351(k) BLA must be submitted no later than June 16, 2023—*after* the Initial Delay Request due date of May 22, 2023. The Initial Delay Request form, however, does not explicitly acknowledge this scenario. Rather, the question of "licensure" only provides four options, under which the biosimilar manufacturer must confirm: (1) it has submitted, and FDA has licensed, its 351(k) BLA; (2) it has submitted, and FDA has accepted for review, its 351(k) BLA; (3) it has submitted a 351(k) BLA, but FDA has not yet accepted the application for review; or (4) it has not submitted a 351(k) BLA.

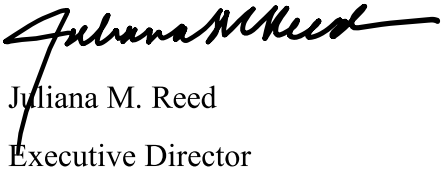
A biosimilar manufacturer that has not yet submitted its 351(k) BLA by May 22, 2023, but intends to do so by June 16, 2023, must select (4). To guard against any inadvertent disqualification of such Initial Delay Requests, CMS should make clear that selecting this option does not preclude eligibility for the Special Rule Delay.

VII. Conclusion

We recognize the tight timeframes dictated by the statute necessitated haste and appreciate CMS's explicit acknowledgment that the Guidance only applies to IPAY 2026. However, we were particularly disappointed to see that CMS intends to use guidance, in lieu of notice-and-comment rulemaking, to implement the Special Rule Delay process in ways that exceed CMS's authority by adding on additional, extra-statutory definitions and requirements.

The future of medicine lies with biologics, and biosimilars provide a critical bulwark to lowering healthcare costs. Even with the program in its infancy, biosimilars have generated substantial savings and have increased patient access to safe and effective, lower cost medications. However, the continued success and sustainability of the biosimilar industry hinges on policies that facilitate competition. As described above, the CMS Guidance poses grave risks to the biosimilar industry, along with the competition and patient access it provides. Although notice-and-comment rulemaking could not cure CMS's *ultra vires* actions, that does not excuse its dispensation of these important guardrails. We respectfully urge CMS to rescind its Guidance, and in particular the faulty interpretations discussed above, and to engage in the formal procedures necessary to ensure appropriate implementation of the IRA, including to preserve the critical functionality of the Special Rule Delay.

Respectfully Submitted



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