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CENTERS FOR MEDICARE AND MEDICAID SERVICES

Medicare Evidence Development & Coverage Advisory Committee

Meeting held virtually via Zoom

February 14, 2023

Centers for Medicare and Medicaid Services

7500 Security Boulevard

Baltimore, Maryland

Panelists

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Vice-Chair

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Guest Panel Members

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Craig A. Umscheid, MD, MS

Richard J. Hodes, MD

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MEDCAC Coordinator

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PANEL PROCEEDINGS

(The meeting was called to order at 10:09 a.m. EST, Tuesday, February 14, 2023.)

MS. HALL: Good morning and welcome committee chairperson, vice chairperson, members and guests, to today's virtual MEDCAC meeting to discuss the analysis of coverage with evidence development. I am Tara Hall, the Medicare Evidence Development and Coverage Advisory Committee coordinator.

For the record, voting members present for today's meeting are Sanket Dhruva, Michael Fisch, David Flannery, Carolyn Ford, Genevieve Kanter, Karen Maddox, Marc Mora, Olorunseun Ogunwobi, Sally Stearns, John Whitney, Ian Kremer and Dru Riddle. Nonvoting panel members are Joseph Ross, Parashar Patel, Daniel Canos, Craig Umscheid and Richard Hodes. A quorum is present and no one has been recused because of conflicts of interest. The entire panel, including nonvoting members, will participate in the voting. The voting results will be available on our website following the meeting.

We ask that all speakers state their name each time they speak, speak slow and

precise so everyone can understand, speak directly into your computer mic, and do not use your speaker phone to help achieve best audio quality. Insure your devices are on mute if not speaking, and while speaking, please place ringers on silent, remove pets from your area and anything else that will minimize distractions and limit background noises.

And now I would like to turn the meeting over to our CAG Director, Tamara Syrek Jensen.

MS. JENSEN: Good morning, and welcome to our second day of our MEDCAC. Just as a reminder, what we ask our panel to weigh in on is that once the CED has gone through the full national coverage determination process as outlined in the statutes and the Agency has made a decision that there are evidence gaps in the evidence, rather than issue a national non-coverage, we have decided to issue a coverage with evidence development.

Today we've asked the panel to give the Agency guidance on the coverage with evidence development criteria for any such request that was presented to the Agency to

approve. Any comments that we had on the process, or anything outside of what we've asked the panel to weigh in on, we are taking all those comments internally and we will discuss how we can improve our national coverage determination process.

Again, thank you to everyone that commented yesterday, we did appreciate all of those comments and again, deep gratitude to the panel on sharing both of your days with us and giving guidance to the Agency on these very important issues. Dr. Ross?

MS. ROSS: Thanks, and welcome back to everyone who is here today. I think we're going to have a pretty eventful, or maybe not eventful but it will be an insightful discussion of these various criteria.

Just for the audience, a reminder that while we would like to be in a position of being able to tell CMS when they should issue a decision on a national coverage determination, we are only here to give them advice on the criteria that they should be using when the decision has been issued, how can those studies be best designed and reported in a way that

helps CMS design a program that makes the best decisions for its beneficiaries on the product under consideration.

We have an opportunity in the beginning of the morning to reflect on the many excellent public comments we received yesterday, we will open that in a moment, and then we're going to move to a formal voting process.

This will feel a little sort of staged in the sense that we will be walking through each of the criteria that the proposed part f the AHRQ report that was presented yesterday by Dr. Jodi Segal. For each criteria that was proposed, I will read through the question as the criteria originally stood and is now being newly proposed. I am literally going to go around in the order by which people are listed on the committee roster, ask people to vote and ask people to explain their vote. So etch time we're going to be walking around in a circle, just so everyone is aware of that, what the format will look like, all right?

But we have an opportunity to begin the day just by reflecting on the information

that was presented to us yesterday, and again, I don't know if people have points of clarification that they'd like to ask either among each other on the committee or to others. I would encourage us to try to keep the conversation among us, which is more typical, but obviously if there is an important point of clarification, you can ask.

I'll just open it up to the committee to start to see reflections on the day that they want to say aloud, and/or questions for clarification. Remember to use the hand function on your screen. Mr. Patel?

MR. PATEL: Thanks, Dr. Ross. So this is a question again, I'm not sure of and I'm kind of curious. What's the definition of contemporaneous comparison group? And I ask that because, you know, frequently in clinical studies you have objective performance criteria based on a similar cohort of patients that may have already had the intervention and you're using that instead of a comparison group, and also it goes from as mentioned, placebo. So would looking at a relatively recent cohort of patients that have undergone similar

interventions in those studies, would that qualify as what Johns Hopkins and Dr. Segal was thinking about, the words contemporaneous group? I don't know if that question made sense.

DR. ROSS: It does. I think it's essentially saying, you know, that the group is being enrolled at the same time, by time, and that if that group is not included, that just needs to be justified or explained why a historical color would be used. It doesn't explicitly say that that comparison group has to be enrolled in the same study; I suppose you could, you know, speculate that it may be, but those people could come from sort of a real-world data source for lack of a better term, and that their observations are being seen in real time, but I think more likely they were kind of enrolled at that time, that's my interpretation of it.

DR. FLANNERY: The is Dave Flannery, I couldn't find my raise hand icon, and I had a question on a requirement from yesterday.

DR. ROSS: Yes, of course.

DR. FLANNERY: It was requirement R in

the report from AHRQ and question 17 on the voting questions, and I'm not sure I understand requirement R. It seems to be more like a negative statement rather than a positive statement and I don't quite understand the importance or value of that. I think Dr. Segal would be the best person to explain that.

DR. SEGAL: Hi. This is in response to what was the initial requirement, initially it was I, which did talk about studies to test toxicity, so we felt like we needed to include some reference to toxicity to be consistent with the initial set of requirements, the phrase or two that we thought were particularly unclear in the initial requirements that talked about testing the pathophysiology in healthy individuals.

DR. ROSS: Dr. Segal, thank you again for being with us. It completely escaped me that you would be with us again. If you want to address Mr. Patel's question about contemporaneous controlled and if I interpreted that correctly.

DR. SEGAL: Up did fine, Dr. Ross.

DR. ROSS: Dr. Fisch?

DR. FISCH: Since sponsors/investigators seems to come up in several of the items, I found myself a little bit puzzled about why they weren't distinguished, but I found yesterday's conversations, you know, pretty helpful. And essentially, I guess I imagined that in a given protocol, I imagined like the face page typically has the investigators, you know, the principal investigator, coinvestigator, lead statistician, you know, substudy chairs, and so I was thinking of that as investigators, and then the sponsors could be fully employed researchers or part of that study team, but not always and typically not. And then there is site investigators, the people who are, in multicenter studies are involved.

But in the end for our purposes, it seemed like investigators don't get named right from the beginning of this process, and the way I ended up thinking about it is just think about the sponsor really as the key word, the sponsor and their chosen set of investigators whenever that takes shape. This is just reflecting on how I processed some of that

yesterday.

DR. ROSS: Dr. Kanter?

DR. KANTER: Yes, this is a question for Dr. Segal on criteria Q, I had two questions related to that.

The first relates to the sharing of, quote, analytic outputs and analytic code with CMS, and I assume that's to support replication to include data in the output. Is that everything that's required to do the replication, is the first question. I'll pause.

DR. SEGAL: Right. So no. In one of the interim versions we did, we said that investigators would commit to sharing the identified data. After it went through the public comment period, though, we removed the sharing of data in response to those comments because we thought it would make recruiting participants too difficult, so that was the rationale.

DR. KANTER: I see. So then the sharing of these things would then, without the data, it seems like that sort of weakens whatever replication efforts there might be, or

unless replication is totally out, if I can clarify?

DR. SEGAL: Right.

DR. KANTER: Okay. Secondly, the part related to HIPAA, and in this earlier criterion it had data governance and data security, and I noticed the governance, privacy issues under governance, so it's governance and then privacy and security. I assume that the reason that's not there is because the code privacy had to account for stipulations related to data privacy under the new criterion, would that be a good assumption?

DR. SEGAL: Right, we though it would be separate.

DR. KANTER: Good, thank you.

DR. ROSS: Mr. Kremer?

MR. KREMER: Thanks. So two questions for Dr. Segal, and I just want to start by thanking Dr. Segal again for really excellent work under very difficult circumstances, and I will try not to make the circumstances more difficult with my questions.

So apologies if this has been asked and answered and I missed it or didn't absorb

it, but in the second criteria where there is reference to timely completion of the CED process, do I understand correctly that that is subject to a negotiation in any single CED, that would be subject to negotiation between the sponsor or investigator and CMS, ultimately CMS is the unilateral decision maker about what timely completion means, and that's a responsibility solely oriented toward the investigator or sponsor, it's not requiring CMS to complete an end of the bargain, if you will, if reconsideration based on the successful completion of the trial and submission of a reconsideration request, right?

DR. SEGAL: I guess it's how you interpret it, how you think that if the milestones are to be met, CMS has to do their part as well, or they won't be met.

MR. KREMER: Okay. Just so that I understand, that would be the logical explanation and expectation, but it's not actually required and articulated anywhere in the report as a proposal, right? So a sponsor could do everything that had been agreed upon, sponsor or investigator could do everything

that was agreed upon at the outset with CMS, but the report and these recommendations don't include any actual structure or articulated mandate, or voluntary on the part of CMS, articulation of a timeline under which CMS will then engage upon a formal reconsideration, obviously the outcome of which would be subject to the interpretation of the evidence, that is not a part of the AHRQ report, recommendations, voting questions today.

DR. SEGAL: That's right.

MR. KREMER: Okay, got it, thank you.

And then the next question is our fourth voting question which I suppose is probably item D in the report, and there's this reference, we discussed it a bit yesterday, about net benefits. Do I understand from the report that you generated and yesterday's discussion, net benefit is purely about benefit to patients, it's clinical benefit, it's not economic benefit, it's not cost saving, it's not the triple lane or any of that, it's purely, it is patient benefit where patients as a class benefit from this therapy, service, et cetera.

DR. SEGAL: Right.

MR. KREMER: Okay. Is that articulated as such in the report and I just missed it, or is that just your and my interpretation of what net benefit ought to mean?

DR. SEGAL: I think it's in D, the primary outcome is for clinically meaningful differences.

MR. KREMER: Okay. All right. Thank you.

DR. ROSS: Dr. Segal, can I just follow up on Mr. Kremer's question? When the report was being generated, the milestone issue which came up a bunch yesterday and just to get to it, was there ever a discussion about adding a milestone after submission of the materials to sort of have a follow-up meeting to discuss the results with the Agency, just as a question, as one of the milestones?

DR. SEGAL: No.

DR. ROSS: Or was a specific milestone discussed?

DR. SEGAL: Specific milestones weren't discussed, including any meetings,

that's not part of it either.

DR. ROSS: Okay.

MR. KREMER: Joe, I apologize, just a very quick followup, not an interrogation, just clarification. Dr. Segal, in your last response to me you were saying that the net benefit should be interpreted as the clinical benefit to the patient because of the reference to clinical meaningful difference, correct, and so that's putting D and E together, seeing them as conjoined twins if you will. Is that correct, is that why you're making that point?

DR. SEGAL: Sure.

MR. KREMER: Okay, thank you. Thank you, Joe.

DR. ROSS: Sure. Dr. Canos?

DR. CANOS: Good morning. Just a bit more clarification with respect to the wording on the HIPAA aspects. In thinking about the target here, sponsors, investigators and their commitment on the data side, I'm just trying to understand the target of the wording here in compliance with applicable laws. Are we viewing HIPAA as a point to sponsor/investigators, or are we thinking more

so about governance and security data provisions, recognizing that some of the individuals collecting the information, providing information where HIPAA would be applied, you know, health plans, clearing houses, the providers themselves where HIPAA would be applicable, as opposed to sponsors and investigators as not the ones directly providing care would be the ones that have to be following the rules in requirement B, and in any of the governance and security provisions that would be kind of imparted upon that.

What are, you know, bottom line, I'm wondering if it would be best to close out the words even after below, and then HIPAA would specifically apply to sponsor/investigators in this case with the requirements.

DR. SEGAL: I would say honestly, we didn't think it through in that detail. We felt like we needed to keep all of the regulations that existed in the initial set where they were.

DR. CANOS: Okay, thank you.

DR. ROSS: Mr. Patel?

MR. PATEL: Thank you. So I have one

specific question and that is a general observation/question for Dr. Segal. I'll get to the specific one and then get to a general one.

Criteria N, which discusses sponsor/investigators describe plans, and then the phrase as motivated by existing evidence? Typically folks might say based on existing evidence, and I was struck by that wording versus based on. Was there any reason or am I reading way too much into the words?

DR. SEGAL: I don't know why it showed up like that. That seemed to happen after the KI discussion. I don't know.

MR. PATEL: That's fair. And then the broader question is, you go through the criteria, some of the criteria described sponsors and investigators having to this, other criteria you talked about the protocol does this and you know, you could look at for example, in criteria D the references to sponsors, investigators; criteria F talks about the protocol describing something; criteria C doesn't talk about any of those. Were there conscious choices made there or was it just to

make it flow so you're not saying the protocol does this in every criteria? Again, maybe a silly question, but I didn't know what to read of the changing actors, right, in the different criteria.

DR. SEGAL: It was not done with a lot of intent.

MR. PATEL: Thank you.

DR. ROSS: Little did Dr. Segal know that we would be asking about the intent of each individual criteria.

DR. SEGAL: That's fine.

MR. PATEL: The words are important because if this is going to be policy or some aspect of it, I just want to make sure the intentions are clear, right?

DR. ROSS: Absolutely.

DR. SEGAL: And remember too that CMS made wording changes too, that aren't necessarily documented exactly in this document.

MR. PATEL: Great.

DR. ROSS: Dr. Stearns?

DR. STEARNS: Excuse me. I just want to get back to Mr. Kremer's point briefly about

net benefit, in that I know it's out of our arena to consider cost and value and I think we're all clear on that, but the focus was very much on the patient. Are we to from a patient perspective consider that to include patient family and caregivers also?

DR. SEGAL: Yes, I think we always would.

DR. STEARNS: Okay. I just wanted that for clarification.

DR. SEGAL: Thank you.

DR. ROSS: Dr. Dhruva?

DR. DHRUVA: Thanks. I wanted to follow up, Dr. Segal, thanks for helping us better understand item Q. So Dr. Kanter's question brought up to me what seems like an important gap where the data are not shared with CMS or a trusted third party, and this leads to me to a couple of questions.

One is, and I know we discussed this a little bit yesterday, but what is, what does that trusted third party, are you able to sort of provide an example or two of what that might mean, and yeah, I guess, I think that would be helpful, and would there be any expectation

that the actual raw data would be shared with that third party if not with CMS?

DR. SEGAL: So right now it doesn't say the data would be shared, and I think the third party would be a contractor of CMS, some analytic shop.

DR. ROSS: Okay. Mr. Kremer?

MR. KREMER: Thanks, Joe. Dr. Segal, I want to draw attention to, I think it's recommendation J, reflects the demographic and clinical diversity, that item, that voting question. So first of all, thank you for addressing this, I imagine we all agree and firmly so that health equity has to be at the center of American health policy and practice, and I will just note for the record, my organization has worked, I hope tirelessly, we certainly try to work tirelessly to encourage NIH, FDA, CMS, other stakeholder government organizations and certainly the private sector and the patient and family communities of advocates to prioritize that issue. But I do want to understand what the implications are for this voting question is in the context of CED and your report.

So does the report articulate a standard by which reflecting should be measured, what reflects and what fails to reflect, is there a formula that's proposed, does CMS already have a formula? I understand it can't be one size fits all because different health conditions have different rates of incidents and prevalence, but is there a system that CMS uses to determine what does reflect, what level of inclusion would meet or exceed reflecting that diversity, or are you proposing any method or metric on which CMS could then calculate it, so that there's clarity between not only investigator/sponsor and the Agency, but frankly more important, the consumer public, the patients and to Dr. Stearns' excellent point, family supporters of patients will understand whether a CED study is going to actually achieve results that would be considered reflective and representative, and therefore be eligible for a potential reconsideration process?

DR. SEGAL: No, we couldn't really include the operationalization of all the requirements in this document, so it's probably

up to CMS and the sponsor/investigators to discuss what that looks like, and I imagine it would be described in the protocol.

MR. KREMER: Okay. So there is not an existing standard that you're aware of that CMS uses, or a set of methods that they employ to set that, this is forward looking purely?

DR. SEGAL: Right, not that I'm aware of, but there may be.

MR. KREMER: Okay. Well, I'll give up the floor in a moment, Joe. I would just say it would be very helpful for forward looking if CMS could articulate for us or for the public later the method they will use when they are trying to come to a determination with a sponsor so that we understand if this is practical and achievable, or if it's just an academic discussion, an ideal that there is no plan to actually achieve. Because it's where the rubber meets the road for particularly overrepresented and under included communities across various aspects of demography that we ought to concern ourselves with, how does this get operationalized rather than philosophically, is it a valid point.

DR. ROSS: Thanks. Dr. Maddox?

DR. MADDOX: Thank you. So first I'd just like to voice my support for the folks who have raised concerns about the lack of inclusion of data in the things that will be shared. I think that's a pretty significant decision as to whether or not data would be shared, and while I certainly appreciate that it's important to encourage people to participate, to the degree that we're moving towards data collection as part of the delivery of clinical care for real-world evidence or electronic health records to claims, Medicare already has the data, they have data on everything they pay for, so to some degree I think that expecting that the group who is doing the paying will, you know, receive the information that they need about the patients is not quite the same as saying that you will share someone's personal data around, you know, sort of unrelated items.

So I think we should really at least consider encourage that the criteria opens the for inclusion of data. I feel strongly that it should be included, that may not be everyone's

opinion, but I do think it's a really important decision.

My second comment is something I don't know the answer to and I'm struggling with, and wonder if others are that might come up in our conversation this morning. The idea of the timing of the creation of additional evidence to evaluate coverage seems crucial, and I'm not talking about the out of scope part about the decisions that CMS makes, I'm talking about the degree to which the studies are actually timed appropriately. If you're trying to use real-world evidence to understand who, the benefit of something, it's quite difficult to do once everybody's getting it, so you could not do a TAVR versus SAVR comparison once that can be everywhere, because the clinical decision about who gets what is going to overweigh the -- outweigh the differences in the clinical efficacy of each of those choices, right?

But initially, before it was everywhere, you would have sort of plausible comparisons where the only reason people weren't getting it is because it wasn't at

their center, not because they weren't a candidate, whereas now if you don't get it and you're otherwise as far as we can tell a candidate, that's clinical decision making and you can't use that to generate real-world evidence.

So it seems to me that there ought to be at least some phrasing in here that talks about encouraging the studies to be, contemporaneous isn't right, but like early or timed immediately or something like that, so that it really is saying that we expect that part of this is that people are going to plan to start collecting data out of the gate, both because the data will be better, and also because we have an expectation that there are going to be decisions made contextually around the future coverage.

So I've just been struggling with whether that fits in anywhere here or not, but I do feel that the time limits of the data is an appropriate part of whether it's useful, frankly, for this type of study. Thanks.

DR. ROSS: Dr. Segal, did that come up in conversations, or do you want to address

that?

DR. SEGAL: No, it did not specifically come up.

DR. ROSS: Okay. Dr. Canos?

DR. CANOS: Thank you. I did want to just get a little clarity around voting questions in comparison to the slides presented yesterday from Dr. Segal. Specifically, you know, a part of my comments on the questions would leverage the existence of certain sections that don't appear within the voting questions, particularly the applicability of CFR part 45, CFR 46, as well as 21 CFR 50 and 56, is it your understanding that those are off the table because those requirements would exist, and we're just voting on one, or commenting on ones that are going to be refined in some way?

I just want to make sure that as I provide comments, it is appropriately referencing requirements that are going to be place even if they don't appear within the voting themselves.

DR. ROSS: Is that a question to CMS? Not -- I guess I would, I'm stumbling a little

bit because I'm looking at the scoring sheets and only seeing that what we have in front of us. Tamara, do you want to jump in?

MS. JENSEN: I can answer, yeah, yeah. So Daniel, I think that's exactly right, those are legal requirements that we would not remove, because those are things that, I don't have it directly in front of me but you know, you've got team subjects, you've got various FDA regulations, you have HIPAA statutes, all of those must be followed.

DR. CANOS: Thank you. And that is super helpful, you know, it affects a lot of my comments here about us adding in wording for HIPAA if it's already baked in as well as, you know, some of the other data elements such as data privacy, et cetera. So knowing those that exist help me and hopefully the other panelists know what we, where we should be commenting on this. Thank you.

DR. ROSS: Thank you. Dr. Ford? You're on mute, Dr. Ford.

DR. FORD: Hi. Yes, I wanted to just follow up on a comment that was made yesterday by Dr. Segal regarding the possibility of

generating a secondary document that provides more detailed explanations about the intent of the wording that's in the proposed wording. Is that something that ought to be done or is that an idea that's just on the discussion? The secondary document would provide more clarity about the intentions of the new wording.

DR. SEGAL: It wasn't something that CMS asked us to do, so that would be up to them.

DR. FORD: Okay. So would we be making a recommendation to CMS that that particular document be generated?

DR. SEGAL: It isn't one of your voting questions, but Dr. Ross?

DR. ROSS: Yeah, Dr. Ford, that's not an explicit voting question but if it's explicit context which we can offer, which is to say these criteria, you know, would benefit from almost like I an E&E explanation for each individual one or something, and CMS can take that under advisement as they prepare a final policy that would then be put out for public comments, essentially, right? So they take our advice into consideration, then they decide

whether or not to adopt the criteria as proposed plus our comments, they then finalize a policy document that goes out for public comment before any criteria is finalized. So there's opportunities you all along the way. Does that make sense? Great.

Dr. Ogunwobi?

DR. OGUNWOBI: Yeah, I'm going to give Dr. Segal a break and maybe ask for clarification from maybe yourself, Dr. Ross, or someone else. As I've been reflecting on all of the comments, I think it's good for me to just clarify again, as we vote on the requirements, would it be appropriate to vote essential for something I highly agree with and don't want to suggest any change, and then maybe to vote important or not important for things I would want to recommend change? Is that the correct way to approach this as we approach voting?

DR. ROSS: Well, I think there's a certain subjectivity and everyone may approach this a little bit differently. My impression, and having participated in prior meetings, is it's not about complete agreement, it's about

whether the criteria is not important, important or essential, and then just clarify how that criterion as proposed could be strengthened or perhaps goes, you know, is inappropriately worded, say as if to say information, a criteria related to the communication between CMS and the study team is essential, but as worded this criterion could be strengthened by blah, blah, blah, or you know, it's not necessary to require blah, blah, blah. That's how I have generally approached it and again, for the audience also, when we've been tasked to vote on these criteria for CMS in our advisory role, while the voting itself provides value, the most critical part is that there's a court reporter that's recording all of the comment that we make that are then transcribed brought back to the entire coverage team for their synthesis, deliberation and discussion.

And so I would just encourage every committee member to speak out loud the thought they're having as they're making their vote, and why and how the criteria are important or could be made slightly different. Does that

make sense?

DR. OGUNWOBI: Yes, that's helpful, thank you.

DR. ROSS: Dr. Riddle, I have you next.

DR. RIDDLE: Good morning, thanks. Dr. Segal, I appreciate all the work you and your team have done. I have a question for you regarding the reporting criteria, and the language that we're being asked to vote on is that the study is being submitted to peer review with the goal of publication, and I wonder if you might, if you can think back to sort of some of the deliberations that you and your team had around this sort of compact statement relative to the current CED requirements. And I'm thinking along the lines of public availability, and publication bias when you have negative or insignificant results, which potentially wouldn't be as appealing to editorial boards and the like. So was there some conversation that you had around if it's not published, then what, and where do those results live so that they're sort of in the eye of the public and the scientific

community?

DR. SEGAL: So, we would expect that results are posted on clinicaltrials.gov because all of these, whether they're trials or cohort studies, we're encouraging be posted there, so I think there will be a record there. Back after the KI panel discussion we favored peer review for vetting rather than public posting. But you know, we went with the compromise that you should submit it with a plan for peer review, but that it should also be publicly posted, so that it's accessible.

DR. RIDDLE: Great, that's helpful. Thank you very much.

DR. ROSS: Mr. Patel?

MR. PATEL: Thank you. I think the criteria overall are relatively general. I know we're asking for more specificity here and specificity there, but I think one thing to perhaps keep in mind is, you know, having broader general criteria might be more helpful in a policy context where situations come up later and you can't then get yourself out of something that might be tightly defined, no matter how much you might want to, so giving

CMS the broader flexibility, I think is probably helpful to, frankly not just CMS but manufacturers and sponsors.

For example on the data requirements, believe it or not, there's a current real-world evidence CED in which the sponsor can't by contract with a third party turn over Medicare claims data back to Medicare. It boggles the mind but those are the types of contracts that are there, and so I think we ought to be careful about trying to impose requirements, if you will, on data submission, because that might actually handcuff study sponsors and manufacturers and others.

You know, a similar thing, I think on the timeliness of the data, I completely agree with Dr. Maddox that you know, the time period in which it's collected and the technology is disseminated widely to groups out there, so I think what might make more sense, and this might be out of scope but I'm going to make this process suggestion, because what CMS I think typically does with CED today is it will issue the CED decision and they will indicate that the proposed study meets the criteria, the

current criteria, and I think what might be helpful to everybody, study sponsors, the public, manufacturers, and even CMS, is in the decision memo maybe, you know, it doesn't have to be paragraphs and pages, but provide some insight into each criteria for why this particular study met the criteria, right? And I think that would establish a good, if you will, case bump, and provide the public and others with the context of why they made this decision to allow this type of study versus another one. So that's just a general thought.

I think that would also, frankly, provide confidence that CMS's decision making is consistent across technologies, and varies maybe because of clinical perspectives, et cetera. So I think that might be helpful, a little bit off scope but I put that out there because I know CMS is listening.

DR. ROSS: Thank you, Mr. Patel, for making those comments.

Dr. Stearns?

DR. STEARNS: I have two comments on prior comments that have been made. First, I appreciate Dr. Riddle's point. And one comment

that I plan to make on one of the criteria is that there are some journals that are actively working to reduce publication bias from failure to publish negative findings, so I think this has the potential to be very beneficial.

And second, I really want to endorse the points that were clearly made by Dr. Maddox, because I think those are really important, and Dr. Patel just emphasized some of those points. Thank you.

DR. ROSS: Thank you. Dr. Kanter, your hand went up and down, I had meant to call on you before Dr. Stearns. Did you still have a question?

DR. KANTER: No worries, yes. I had some second thoughts but well, since I'm on, I might as well ask. It was in relation to -- actually, why don't you go ahead to the next speaker while I find it.

DR. ROSS: No problem. Dr. Canos?

DR. CANOS: Thank you. You know, reflecting back on comments yesterday, you know, in thinking about the wide ranging that the CED covers, I think there was a substantial focus on postmarket data collection alone, you

know, after FDA market authorization, and some mischaracterizations of programs like the breakthrough program where FDA may consider the nature of data to be collected in the postmarket setting, or the premarket where they extend all that uncertainty where appropriate in the benefit-risk profile type of approval. So I think it's important for us to think, you know, as we look at the CED more widely than post market, we'll go back through and correct the record as far as the characterizations of the FDA side. But I do want to say that you know, I think we've heard from both, it looks like Dr. Brindis yesterday talking about the importance of CEDs more widely and taking evidence generation and providing clarity to innovators in the field and providing those innovations to Medicare beneficiaries in, you know, in an appropriate level of access and a timely fashion.

So in thinking about yesterday, thinking about the criteria, I think I really heard some great comments from the panelists about how do we have this efficient level of specificity and rigor scientifically, while

providing flexibility, understanding that these aren't just postmarket requirements for data collection from the FDA side that inform, you know, coverage decisions in the future. But also, you know, IDE studies, premarket studies where, you know, CMS is shaping the totality of the evidence generation and providing that clarity in this space.

DR. ROSS: Thank you for making that comment. Dr. Kanter, did you want to jump back in?

DR. KANTER: Yes. I actually now have three questions, this is what happens, so the first one relates to criterion E for Dr. Segal. I just wanted to clarify, so originally the existing requirement was that the study has a protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements. So that is no longer part of the criterion and just wondering, was that part of that decision to split up different elements of the protocol into different criteria, or is that significant somehow, its removal from this criterion?

DR. SEGAL: No, I think that shows up

elsewhere with -- well, when we talk about the written plan with the milestones, and then also in F, saying the protocol, what the protocol describes. Maybe there isn't specifically a call for a protocol --

DR. KANTER: I'm just thinking about the Medicare standards, the data sources, key outcomes, key elements of design. I mean, they are all sort of in different parts of the document, of the criteria but yeah, just wondering about its removal from this criterion.

DR. SEGAL: Oh, well, no. In E, the CED study is registered, and a complete protocol is delivered to CMS. We thought H was a little funny because it's self referential, right, because the Medicare requirements are the ones you're reading right now, which seems a little awkward.

DR. KANTER: And then complete protocol, the elements are not specified?

DR. SEGAL: They are not. They are not.

DR. KANTER: The second question relates to, you know, the diversity criteria,

and I think there are a couple of them. I'm not sure if we want to address this in the criteria themselves, but I think it may be possible to do age and gender. I think socioeconomic status at an individual level, as Craig mentioned yesterday, is a bit tricky but probably at a ZIP level code. Racial and ethnic backgrounds, I wonder depending on the group if there might be some power issues, especially related to, you know, populations or conditions where there may be difficulty in recruitment. I wonder if there were some discussions related to that and how we might think about that.

DR. SEGAL: Well, again, that was largely in response to the public comments, because after the KI panel we said population reflects the demographic and clinical complexity of Medicare beneficiaries, without defining in more detail. The public commenters suggested that it be more explicit about what those characteristics are. That's the rationale really.

DR. KANTER: Thank you. And the third relates to the timing, which I agree the

timeline of the data being collected. I do worry from just a general high level point of view that, you know, as some of these, there might need to be more structure related to the use of the data for decision making purposes, because that could also compromise the validity of the trial for, you know, the study that's being run if we prematurely release data, so that's just one thought to the need for the timeliness of the release of the results of these studies. Thanks.

DR. ROSS: Not seeing any other questions, I was going to ask one. I generally wait to make sure committee members aren't going to ask this, but I have one question for Dr. Segal around the I, the primary outcome issue where you say the primary outcomes for the study are clinically meaningful and important to patients, which I presume to mean Medicare beneficiaries, but I did want to clarify if discussions were had as part of the criteria tempt, given that this is an older populations or often disabled population, and discussed as a part of the clinical meaningfulness, not just to the patients or

beneficiaries themselves, but to the caregivers.

DR. SEGAL: Right. Not explicitly, but I think in our head we do think about patients and caregivers, but you're right, not explicitly discussed.

DR. ROSS: Okay. Mr. Patel?

MR. PATEL: Thank you. So I'm going to go back to the timelines because I think, Dr. Kanter, maybe you can clarify, or even Dr. Maddox who raised it originally. Are you talking about the timeliness of making sure that the study when it's completed, the data is either released or published timely, or were you, I thought the conversation initially was about beginning to collect the information and then you will start the study in a timely manner, because then I have a follow-up question or a point I think, particularly on the first one.

DR. MADDOX: I can speak for myself. I was referring to the data collection issue, I was thinking of the criteria about the data quality, that we should encourage timeliness of the data as a component of data quality. I

don't disagree with the other, but that's the one I was talking about.

MR. PATEL: Yeah, so I think on that one, you know, again speaking from the industry side, the context here I think is important for us to recognize, because without CEDs, it very frequently actually goes into the market and sells the device, particularly for Medicare patients, and so most of the time companies are usually eager to get the CED decision quickly after FDA approval and get the studies going, so I think there may be a little bit less concern at least on the industry part of delaying that, and then particularly with many of the novel interventions, I understand the concern that it becomes more challenging to find a comparator group, if you will, once it's disseminated, but I think one thing to keep in mind is frequently with medical devices in particular, but it may also be true in other new services, et cetera, training provisions for healthcare providers in a new technology also takes time, and so that's just another thing to weigh, right, but I completely understand why you would want to provide that

context. And I wasn't sure whether timeliness of a study could have any relevance, but I'll just put that out there as a question for others.

DR. ROSS: Dr. Kanter?

DR. KANTER: Yes, thanks for that clarification. I appreciate it, and maybe I misinterpreted Dr. Maddox's suggestion of sort of release as the trial or study is taking place to facilitate the decision making, and so if the study and the results are absolutely on board with timeliness of the data collection.

Second question, actually for Dr. Canos at the FDA. There, you know, there have been some claims made that the, and you might have mentioned this before and I apologize if I missed I, that, the claims made that the criteria for post-approval studies for the FDA are, you know, may be different from what's proposed for a CED. I wonder if you could address those claims.

DR. CANOS: So not exactly holding the particular conversation to which you're referring, but I would say, you know, as far as the post-approval studies from the FDA side,

there was, I think we heard from Dr. Bockstedt from Medtronic yesterday about aspects where actually FDA collaborated with CMS and the stakeholders to align an evidence generation that made sense, right-sized, you know, studies, actually a tiered approach where Medicare leveraged the existing FDA kind of clinically rich Chin post-approval study, and on top of that layered a claims-based study that captured the wider Medicare beneficiary performance within claims, and was additive to kind of the deep dive clinical study. So I think there have been success stories there.

Also with Dr. Brindis, you know, I think we've heard him discuss left atrial appendage closure registry, where postmarket data requirements aligned within the registry infrastructure and FDA worked very closely with CMS as well as professional societies and with industry and patients to align as far as the evidence generation collection there.

So where appropriate, where possible, we work together on the evidence generation so it's additive and not duplicative in any form, if that was getting to the question raised, or

is there a separate aspect you wanted to touch upon?

DR. KANTER: No, you answered it very nicely. Thank you.

DR. ROSS: That was helpful, Dr. Canos. It does suggest, you know, this kind of interesting opportunity for collaboration between agencies, which is well beyond our purview bit it does, as it relates to the criteria suggests, as Mr. Patel said, an opportunity for flexibility, so that it does, you know, it's not so overly restrictive that it would preclude those retypes of collaboration between the two agencies and whatnot, but that sort of thing elaborates it.

Dr. Canos, you had a question?

DR. CANOS: I do, and sorry to be the noisy gong on this, but would it be possible as we provide our comments during voting for us to see which of the requirements are that we're not voting on that are set in stone just so we can say okay, you know, I'm making these comments, but we've already put out there these requirements are set, just visually. I understand kind of theoretically which ones

those are per se, but it would help me as far as the comments go if those would be possible to put up on the screen.

DR. ROSS: We can't put them up on the screen as I understand it, because they have to be able to see us, but I think it's available as an appendix in some of our material, and maybe Tara Hall can recirculate the old original criterion that Dr. Segal used as a starting point. That's sort of an A through M list of criteria.

DR. SEGAL: Well, I'm sorry, Dr. Ross, but I think in the full report, Table 5 is the final version.

DR. ROSS: Oh. So now A through S, is that right, Dr. Segal.

MR. BASS: Yes.

DR. ROSS: So it is there for individuals to see. I haven't cross-checked like our voting questions versus which is which, but I can try to do that during a break.

DR. CANOS: Yes, so specifically, we do have A through S from Dr. Segal's presentation in front of us. My specific question is, in that presentation, I understand

we are not voting on S and S is going to be a requirement that persists. But I'm wondering which other lettered requirements are not being voted on and are going to be, you know, existing criteria, you know, just so I understand which of these other ones that we're commenting on or voting on are possibly duplicative of ones that are going to be standing that we're not considering today.

DR. ROSS: I think we're voting on every other one than S. That's my memory but perhaps Tamara, if you want to clarify?

MS. JENSEN: Let me take a look at them, Daniel, and let me get back with you and confirm specifically which ones you will not be voting on because those are statutory issues, you know, that we will not review, versus the scientific criteria.

DR. CANOS: Okay, that's super helpful, in particular as I'm commenting on, you know, the aspects for, you know, governance, question number three on where there's no existing portion of governance and data security provisions, you know, if they're otherwise covered by S, that would affect the

way I comment there. And additionally there's reference to data sharing and HIPAA, and that would also affect my comments if there's an element S there that covers aspects of HIPAA.

So that's the nature of the question. It informs where I go on the commentary on the criteria we'll be discussing.

DR. ROSS: No, I appreciate that clarification. I did just count them up and we are voting on 18 and there are 19 listed in Table 5 and I know we are not voting on S, so I do believe we're voting on all of them except for the very specific code, authorized code under which the criteria have to be, so thank you.

DR. CANOS: Thank you.

DR. ROSS: Mr. Kremer?

MR. KREMER: Joe, were you ready for overarching comments or are there any other specific questions you want to entertain first?

DR. ROSS: I think we're actually about ready to transition, actually start getting through the specific criteria one by one. I would, if anyone on the committee has any sort of overarching thoughts that they want

to issue kind of before we get started, now is a great time. Do you have any?

MR. KREMER: I sure do. Okay. So I will just acknowledge, as for I'm sure many of us, this is deeply personal because it's real, this is not, as we all understand, an academic exercise, a set of philosophical discussion, this is about how this gets operationalized for Medicare beneficiaries, often who face high burdens of unmet need.

So I have taken a little bit of time just to jot down a few thoughts, and I apologize for reading off my screen, but I wrote this down because, and this is part of my extended apology, my voice may break during some of this. My family has been through hell and back with insurance denials in the past that were unjustified, and nothing breaks my heart more than the potential that CMS might intentionally or unintentionally operationalize this and behave like an insurance company, because that doesn't serve beneficiaries the way the law or public policy intends. So I'm just going to read through this and again, I apologize if I just need to catch my breath at

any point.

We are not voting on what we wish the recommendation said or the concept that they represent, we are voting on what the recommendations actually say, so I would urge all my colleagues to speak our piece as we have been for the last day plus about how we might improve on the language, but when we are casting our votes, I would urge us all to vote for what is actually on the page, not what we wish was on the page, and I will reiterate that context matters.

If we believe that CMS uses these tools, these study design requirements appropriately, that should guide us toward giving them authority to tighten the criteria. But if we believe that they are not used appropriately, we should question very carefully whether we want to give them authority or, I shouldn't say give them authority, whether we want to vote in support of the notion that they should tighten these criteria.

Next point, and this one I can't stress enough, the law is the law unless and

until the law changes. So this cannot be about what authority we would like CMS to have or what authority CMS believes it has. It can only be about what authority CMS does as a matter of law have. So we should not support CMS revising the current CED criteria when there is no statutory or regulatory authority for the CED mechanism. There is authority for the NCD process and I'll address that in a moment, but not for CED as a mechanism. In practice, CMS is using CED to overreach into FDA's congressionally directed authority. CMS's NCD authority is limited to national coverage, national non-coverage and/or deferring to the MACs. That is it.

Until Congress changes the law or proper regulatory processes are followed, CMS does not have the authority for any CED mechanism. The questions on today's voting questions are moot if CMS lacks the authority to have a CED mechanism. But if you disagree and somehow believe that CMS has the authority for a CED mechanism, then before voting to support any tightening of the CED criteria, it is essential to evaluate whether CMS is using

the CED mechanism responsibly and in the best interests of Medicare beneficiaries.

In my view, CMS is explicitly directed -- sorry. CMS has explicitly directed us not to consider that and we ought to ask why. Maybe because as numerous public comments pointed out, CMS is broken, and today's voting questions don't even attempt to fix the real problems. Today's voting questions don't fix CMS prejudging an entire class of drugs before the evidence is even presented to the FDA, much less to CMS. Today's voting questions don't fix CMS's pattern of ignoring formal reconsideration requests, substituting nonexpert judgment for FDA expert judgment, moving the goalposts on CED studies so they drag on for a decade or longer despite strong peer reviewed evidence of substantial clinical benefit, and refusing to identify the specific requirements to meet threshold requirements for a future recreation.

In fact, CED creates a circular process. We don't have coverage because we don't have data, but we don't have data because we don't have coverage. Today's voting

questions don't prevent CED being used as a classic insurance industry utilization management tool. And Joe, I promise I'm very close to done.

If you disagree somehow, if you disagree and somehow are unwilling to predicate consideration of these voting questions on any consideration of how CED is used or misused currently, then I ask you to consider whether a one size fits all system makes any sense. Clearly, CMS is coming after not only accelerated approval but coming after traditional approvals too. Should there be absolutely no distinction in the study criteria based on whether CMS is demanding an RCT, an open-label extension, a broad national registry or something else, should there be no difference based on whether the intended use is on label or off label? Should there be no difference if it's for devices, drugs, biologics, or services? If you disagree and believe a one size fits all approach is perfectly fine, then in conclusion, I ask you to scrutinize each of these voting questions for whether it is precise or vague, whether it

gives clarity and predictability to innovators, clinicians, and by far most important, to patients facing serious and life-threatening diseases and disorders. Would each voting question make life better or worse for people with ultra rare conditions, rare conditions, common conditions, or prevalent conditions?

Joe, thank you for the time. I'm done.

MR. PATEL: Joe, you're muted.

DR. ROSS: Oh. Thank you, Mr. Kremer. Mr. Patel, did you also have comments?

MR. PATEL: Thank you. So you know, as I said earlier, I think generally the criteria are relatively good. Frankly, J, Q and R, CMS did a really good job, I think, of taking apart existing criteria, of piecing them out, maybe putting some parts with others. They are broad, as I said I earlier, but I think it's necessary in a broader policy context, because of the dangers of specificity. I think the key, frankly, will be how the criteria are implemented, right? When the rubber hits the road, how will CMS take the broad general criteria and apply that to the

specific technology and critical therapeutic area, the populations that they're talking about.

And so you know, for example, will we see more CED studies that are similar to the ongoing study for leadless pacemakers? You know, the FDA, as Dr. Canos pointed out, I think they use the historical competitors from what I understand and, CMS augmented postmarket study requirements with claims data to carry out that CED study. So I think if CMS moves more in that direction, I think there's, you know, positive things for the beneficiaries, and the program overall.

And as I said earlier, I think you know, again a little bit out of scope, but just make sure, you know, hopefully CMS will make sure with each study a sentence, two sentences, something that gives a sense of their rationale for why a study met each of the criteria. I think that would be very helpful but overall, I think they've done a good job and hopefully it bodes well for more CEDs, NCDs coming down the line, versus beneficiaries not having access to this technology, because it's more difficult to

collect data, frankly, when there is no coverage in the first place, so thank you.

DR. ROSS: Thank you, Mr. Patel. Dr. Stearns?

DR. STEARNS: I just want to state a note that I hope that the criteria that we end up voting on will enable CMS to improve the process. I think we would all agree that there is evidence that the process has not been, has had problems in the past, so I appreciate the coal of this committee.

With respect to a one size fits all, I actually, things change over time, I appreciate that these criteria are specified broadly. I will have specific comments on at least one of the criteria where I think some distinction by type of intervention may be appropriate, but overall I think the criteria as a group are good. Thank you.

DR. ROSS: Thank you, Dr. Stearns. Dr. Canos?

DR. CANOS: I think the most recent words on, and then the thoughtful approach to, on how these criteria are applied and think about innovation are really spot on, very much

valued. You know, the old research model of clinical studies and, that were returning slower answers to questions and not providing the innovation is certainly not working, and clearly we see from the charge that we have today that CMS wants to think about ways to make more timely decisions be innovative, leverage evidence from clinical experience and provide, you know, meaningful information on Medicare beneficiaries in a timely fashion while providing that timely access to the therapies.

I think, you know, the comments we've heard today from the panel really are looking to provide that clarity on requirements while removing the incentives to development and keeping pace with the innovation. Really, you know, as I mentioned before, I think about the unpredictable and rational driver for development, and balancing out the race to perfection with the importance of timely and relevant outcomes and information for beneficiaries.

So you know, Mr. Kremer, I really appreciate your comments as well as Mr. Patel,

spot on as far as, you know, what our charge has been today, and some of this spirited discussion during the panel today.

DR. ROSS: Thank you, Dr. Canos. Dr. Dhruva?

DR. DHRUVA: Thanks, Dr. Ross. I'd like to echo, I've really enjoyed the discussion with our panel here this morning. I'd like to echo Dr. Canos' and Dr. Patel's comment. I think from what I've seen in my field of cardiology directly taking care of patients is that we've seen patients get access to novel therapies as a result of coverage with evidence development and that's helped me as a practicing cardiologist understand the benefits and risks better, and while also having, ensuring that patients have access to novel therapies, and we've seen a lot of evidence generated.

I think that one of the comments that I want to make is about milestones. We heard a lot yesterday about CED meeting milestones and timely completion of the CED process. What I've seen is that we learn a lot through the CED process, we learn a lot about outcomes that

matter to patients in diverse patient populations who are indeed Medicare beneficiaries who receive the CED mechanism and sometimes we learn that there are harms that are unexpected. As I mentioned yesterday in the left atrial appended occlusion CED, we learned that women have a much higher rate of inhospitable adverse events when they receive LAAO, and that led to an FDA Dear Healthcare Provider letter that was released after a study as a result of the national determination.

So this evidence that's essential to helping inform risks and benefits, that's essential to helping provide access and helping to inform risks and benefits, helping to ensure that patients are receiving safe care, I think is great and I commend CMS on taking this on and looking for ways to strengthen CEDs so that patients are getting access to novel innovative therapies and ensuring that Medicare beneficiaries are going to benefit and have net clinical benefit. Thank you.

DR. ROSS: Dr. Mora.

DR. MORA: Good morning, thank you. Yeah, I wanted to just reiterate this does feel

very personal to I'm sure all of us, as well as to Medicare beneficiaries. I'm not sure I choose to believe that this represents a tightening of the criteria. I see this as an important step, and the ability for me in a room of patients, and for our system, to have a better discussion about risk, benefits and uncertainties of therapy, which I think is a concrete outcome of this effort. So I see this as an improvement and a step forward in expediting the beneficiary access to new treatments. It's putting in place protections for these risks and helps us understand better the use of therapies, so thank you.

DR. ROSS: Mr. Kremer?

MR. KREMER: I'll say much more briefly than my last statement. I'm a huge supporter, I don't know anyone who isn't a huge supporter of postmarket studies. The question is, under what legal authority and who bears the responsibility for conducting those studies, paying for those studies, reviewing those studies, and whether those studies are used as a method of delaying access for Medicare beneficiaries in need who often have

no viable alternative, or whether they are used as a tool to facilitate earlier access.

So conceptually, apart from the issues of legal authority, conceptually, sure, I think it's great and fine that you generate additional evidence beyond what the FDA reviews to rate, but it's, the process matters and the criteria matter, and the legal standards matter, and the timing matters and the rationale matters.

And this may benefit, this structure that CMS has set up, with or without appropriate legal authority, may work much better in one domain than it works in another. I hear what people are saying about devices, and I will tell you the experience, at least from my community, has been radically different on drugs. That's not to say I endorse the status quo of CED used by CMS for devices, it may be a good outcome achieved through the wrong means. So let's get to the right means. Let's get proper legal authority, statutory and regulatory, before we embark on something that some may find useful and may in fact be useful.

But we aren't there right now. That's

my point.

DR. ROSS: Thanks. And Dr. Ogunwobi, you're going to close sort of our big picture comments please.

DR. OGUNWOBI: Sure. Thank you for giving me the opportunity to make one more comment. It will be a brief comment and it will be directed at, I think it was number J, when Dr. Jodi Segal presented, and it's for diversity and inclusion, and I think it is very essential.

I would like to strongly encourage CMS to think about, you know, framing that in a way that really ensures that it accomplishes the goal rather than just be a pro forma or perfunctory think that's listed, and the way to do that is to, you know, specify, you know, the need to have adequate sample size for those diverse groups and those groups that need to be included, and to specify the appropriate metrics that need to be met in order to insure that, you know, folks who are doing the studies aren't just including one or two, and that the adequate evidence is not provided that would diminish disparities rather than expand them.

DR. ROSS: Thank you. Just before, we're going to take a break in a moment just to get the voting system set up.

I do just want to take a moment to note, primarily for the larger audience, all of these comments which are being recorded, there will be a public transcript, or publicly available transcript, or a transcript made publicly available.

I do want to note, you're probably hearing discordance or just disagreements among the advisory committee, and that's deliberate. You know, when we're convening, the goal is to bring together different points of view, and our goal is not consensus, and you'll hear that on the voting. The goal is not what we all necessarily vote the same way, but the purpose is to elicit different points of view for CMS to take into consideration as it makes its policy. So as a group we are not trying to achieve consensus, we're not trying to convince one another. Often when we make public comment, we're making out comments publicly so that CMS hears us as advisors in our recommendations, and I just want to make that

clear.

So Tara, should we take five minutes and come back at 11:30 eastern, is that the goal?

MS. HALL: Yes.

DR. ROSS: Okay, so people who need to run to the restroom and then get back on, we will be back in five minutes.

(Recess.)

DR. ROSS: Can I just ask, has every committee member logged on to the system?

DR. FLANNERY: Not yet.

DR. ROSS: Okay.

DR. FLANNERY: Where is the link? I can't find the link. Which email was it in?

DR. ROSS: Tara will re-email you momentarily.

DR. FLANNERY: Oh, okay.

DR. ROSS: Don't start voting prematurely.

(Discussion between members and staff regarding connections.)

DR. ROSS: And I apologize to the audience as we work out this technical issue.

Tara, good. I was going to say there

was something messy about this screen. Tara, does the voting screen have to be live since individuals are going to be asked to say their votes and explain it, just so we can continue to see each other on the grid?

MS. HALL: We typically have this screen for the audience to see it.

DR. ROSS: Okay. Has every committee member who needs to vote using the online voting system been able to log on?

DR. FLANNERY: I have not received the link.

DR. ROSS: Tara, can you provide the link to Dr. Flannery?

MS. HALL: If you look in the chat, you can see it. Dr. Flannery, do you want me to send you an email?

DR. FLANNERY: No, no, I found the chat. Thank you.

DR. ROSS: Just while Dr. Flannery is figuring that out, just to make sure, I'm sorry, but I'm going to go one by one just to make sure everyone is on the voting system.

Dr. Dhruva, are you on?

DR. DHRUVA: Yes, thank you.

DR. ROSS: Dr. Fisch?
DR. FISCH: Yes.
DR. ROSS: Dr. Ford?
DR. FORD: Yes.
DR. ROSS: Dr. Kanter?
DR. KANTER: Yes.
DR. ROSS: Dr. Maddox?
DR. MADDOX: Yep.
DR. ROSS: Dr. Mora?
DR. MORA: Yes, I am.
DR. ROSS: Okay. Dr. Ogunwobi?
DR. OGUNWOBI: Yes.
DR. ROSS: Dr. Stearns? Do we have Dr. Stearns.
DR. STEARNS: No, I am on. By the way, I got kicked off shortly before the break, but I should be stable, and I'm on the voting system.
DR. ROSS: Okay, thank you. Dr. Whitney?
DR. WHITNEY: Yes.
DR. ROSS: Dr. Riddle?
DR. RIDDLE: Yes.
DR. ROSS: And Mr. Kremer? Did you say yes?

MR. KREMER: Yes.

DR. ROSS: Okay, because now I can't see everyone. Very good.

MS. HALL: Hi, this is Tara. Please do not vote until Dr. Ross asks you to vote.

DR. ROSS: Yeah, if people clicked on something, you will be able to change it in a moment.

So we're now going to move to the voting portion and we'll probably go until 12:15, so we'll see how many we can get through in that time. We're going to go one by one, question by question and again, what I'm going to do is I'm going to read the current CED version from 204 and then I'm going to read the proposed new criteria that came from the AHRQ record, I'm going to ask you to rank the following, that criteria as zero, not important; one, important; or two, essential. I'll give everyone a moment to tally their vote using the online system. When we have a total of 12 I will then turn to everyone individually one by one to ask them their vote and their rationale behind it. Okay? So we have 18 criteria to walk through.

So the first criteria for us is related to the sponsor, the earlier version of the criteria was, the study is sponsored by an organization or individual capable of completing it successfully. The proposed criteria is, the study is conducted by sponsors/investigators with the resources and skills to complete it successfully. Please vote whether this newly proposed criteria is not important, important or essential.

(The panel voted and votes were recorded by staff.)

Great. That puts us at 12 votes. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, and I think that there's an opportunity to strengthen this criteria because I think the goal is for the sponsors to bring the resources, whereas the investigators bring the skills.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted two that this is essential, and I think it could be strengthened by specifying that the study is conducted by sponsors inclusive of their chosen

investigators.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: Two, it's essential, and I agree with the foregoing comments from my co-members.

DR. ROSS: Okay. Dr. Ford, how did you vote?

DR. FORD: I voted two, that the revised language is essential, and I feel that having resources and skills are more specific and would get to better results.

DR. ROSS: Dr. Kanter?

DR. KANTER: I voted two, essential. I understand the distinction between sponsors and investigators, and the differential timing. I think the phrasing gives CMS scope to identify the individual resources and skills that are needed from both parties.

DR. ROSS: Dr. Maddox?

DR. MADDOX: I voted two, essential, and actually appreciate the vagueness of the language, because I think the combination of sponsors and investigators, industry and foundation or other sponsorship could vary, and

so actually I appreciate the vagueness of sponsor and investigator roles in this one.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: I voted two. I think this is consistent with the goals of determining reasonable and necessary services.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two because I agree that this is essential.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted two and I agree with the comments, including that the flexibility in terms of sponsors or investigators is important.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted zero. I think it's unnecessarily specific, that any sponsor or investigator would meet this criteria who could meet any or all of the other criteria, would de facto meet this.

And I'd make a general comment that I think the term sponsor/investigator could

probably be removed from every criteria where it's present; it's unnecessary specificity.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted one, along the lines of actually the comments that Dr. Whitney just made; this is important but the sponsor/investigator leaves perhaps unnecessary ambiguity, and I don't know necessarily adds to the context of the recommendation.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: It will come as a shock to no one, I voted zero for the reasons I articulated above and will not repeat on each of the 18 questions, but that's context for me. I will just say in regard to this particular question, I appreciate Dr. Whitney's point about reference to sponsors and investigators. I think for any study, that's who we would be talking about, and it's constructive to talk about studies being conducted with the right resources and skills, so I would just associate myself with the comments of other panelists about how to perhaps strengthen and clarify

some of the details.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I would have voted probably one along the lines of what Dr. Whitney said. I do agree with both Dr. Kanter and Maddox about the general nature of sponsors and investigators. Many sponsors, in fact, do have the skills necessary to complete studies and you know, there may be some studies in the future of particular real-world evidence where the sponsor and the investigators are one in the same, and so I like the fact that it mentions both without providing resources or skills to one role or the other.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: I would have voted one, important, consistent with the others that have voted in the one category or would have voted in the one category. The evaluation itself of the resources for completion is, it does lack clarity in my perspective, and I certainly do think there's the importance of appropriate

skills and, credentialing to conduct a study, but resources certainly leaves a bit to be desired as far as what we need.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted two. I think resources and skills are both essential.

DR. ROSS: And Dr. Hodes, how would you have voted?

DR. HODES: I would have voted two in the setting of this important criteria, to make sure the study is carried out by agencies, sponsors, investigators best able to determine risk benefit, which is the goal of serving this overall mission. I think that the greatest specificity applied here, with the residual ambiguity, is a good balance.

DR. ROSS: Great, thank you for your votes.

We're going to move to question two, or criteria two. This vote relates to this theme of communication; there was no existing criteria in version 2014 of the CED requirements. The proposed criteria is, a

written plan describes the schedule for completion of key study milestones to ensure timely completion of the CED process. Please cast your votes.

(The panel voted and votes were recorded by staff.)

Great, thank you, all the votes are in. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted a one. I think this is important but not essential because I think there may be updates as we heard yesterday from Dr. Brindis as technologies evolve, as new evidence of benefits and harms emerges, and that CMS will need additional flexibility as a CED process continues.

DR. ROSS: Dr. Fisch?

DR. FISCH: I voted two, that this is essential, and I was really influenced by the public comments yesterday and the panelists' discussion about milestones. On one hand there was quite a lot of concern about the data collection burdens dragging on and this being sort of endless, and the desire for milestones in a way to bring it to completion.

On the other hand, as Dr. Dhruva

pointed out, you know, sometimes long-term data collection monitoring of late effects, late toxicities is important, and so there has to be some balance struck, and I think that Dr. Maddox's point about the pace of accrual in the data collection influencing the interpretation of comparisons is important and could be incorporated into this notion of milestones, and I think milestones can be negotiated and adjusted in the face of some of these findings so I think it could be flexible, but I don't think it needs to be strengthened in any way, I thought it was essential as is.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: I voted two, essential. I think the kind reactive comments that were made about the milestones and timetables need to apply to not only investigators but also to a then timely response to when the study is presented back to CMS.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I felt the matter was essential so I gave it a two, and my comments are consistent with the comments of Dr. Fisch,

especially as relates to the public comments that were made yesterday regarding timely completion of data for this process.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential. It's clear that a timeline is very important for resolving uncertainty for multiple parties, so it's crucial for having CED be effective.

I might add, the revision of periodic updates to be determined by CMS or perhaps even specified here, every two years, every five years, I think that was being proposed, but to incorporate the possibility, in fact possibly the requirement of updates.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted essential. I think this is just part of good study etiquette and hygiene, and I think the public accountability of having a timeline, particularly for beneficiaries awaiting these sorts of data is just good practice.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: Yeah, I voted essential

too, and I agree with comments, I feel like in terms of methods, timeliness and milestones are important components to that. Thanks.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: Yeah, I also voted two. I certainly agree that there needs to be a schedule; I do think it needs to be flexible and a lot of it driven by these with the skills and expertise to determine what would be considered a reasonable and flexible schedule. My vote of two was driven largely also by the comments, the public comments yesterday. We don't want endless studies, we want these studies to have a definite end.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted two for essential. I have a comment and this pertains to the fact that I think the criterion may not be a one size fits all. My comment is that appropriate milestones may vary by the type of treatment or exposure being considered. Some standardization by CMS of the types of milestones appropriate by type of treatment,

for example pharmaceutical products versus medical devices may be beneficial. I also want to note that adjustment to milestones over time may be needed, but should be done in a transparent manner.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted two. I think that as stated by others, it's an essential component of a good study, and it may help with the, avoiding endless or protracted CED periods.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted two, essential. I echo the comments I believe Dr. Kanter made a few speakers ago about the need for studies with specific contextual check-in points as opposed to just a prior laying out milestones, but there may be individual CED determinations that require more frequent or different check-in points. I think it's important to mandate that on the front end but not prescribe it specifically, because what's appropriate for one device, one drug, whatever, may be very

different than what's appropriate for another.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: I voted zero for the reasons that I identified earlier. I will just for context, because we've been told that the comments we give matter a lot more than the particular number of a vote, I would agree with almost everything I've heard from my colleagues regarding this element, but I would again ask us to think about it in context. We all agree, we don't want endless studies, we all agree there ought to be incentives for sponsors or investigators to conduct as reasonably expeditious studies as possible, and have them be robust and really give predictability to not only payers, but more important to the Medicare beneficiaries and other patients.

With that said, these are one-sided requirements and so part of the context for me is this creates requirements that it's -- let's not fool ourselves. This is not a real negotiation, this is CMS telling investigators or sponsors what will be required to potentially get out of a CED eventually. And

so what I would have liked to have seen is context in these recommendations.

Joe, I'm wrapping up and I'll be very brief here. I really needed to see here something that completes the circle for Medicare beneficiaries, which is some predictability, not only about when the study will be completed and concluded in a way that produces meaningful evidence of risk and benefit and other factors, but also when CMS will be required to act on that information, not predetermine an outcome for a coverage determination, but take up a meaningful formal reconsideration process. Without that, you're just asking sponsors, investigators and more important, study subjects to engage in a process that has no guaranteed end because CMS is not under any requirement to complete its end of the bargain because they are not required to actually engage in a bargain.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I would have voted two. I agree with the comments of Dr. Fisch, Dr. Kanter, Dr. Riddle. You know, I -- there

have been mention of new technologies evolving, et cetera, and potentially the need to study those as well, some of the challenges. Again, I would leave it to CMS and the sponsors to decide in what context it may be relevant to pull those next generation in, versus starting new studies. I like the general nature of this, let CMS decide and, calendar-wise, how long in frequency updates, et cetera, so I would have voted two.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: I would have voted two consistent with the aptly stated comments from Dr. Stearns and Maddox.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted two. I think this is an important new addition, this theme of communication is absolutely critical, and I think as much as a schedule of milestones can promote communication between CMS and sponsors/investigators to complete CED decisions in a timely fashion, I think it's a win-win.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: I also would have voted two for those reasons stated. I think it's critical establishing the milestones, communicating them to set on course the most expeditious completion of trials. I think implicit is the notion that they are subject to revision. With that understanding, I'm enthusiastically essential on this one.

DR. ROSS: Thank you for your votes. We're going to move on to the third item, which pertains to governance, and for which there was no existing requirement in the 2014 CED requirements. The proposed criterion is, the protocol describes the information governance and data security provisions that have been established. Please cast your votes.

(The panel voted and votes were recorded by staff.)

Thank you for voting, I see everyone's cast their ballot. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted a two, because I think that governance and data security are

essential, especially as more studies start to leverage more real-world data.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted two. This is essential for the same reasons as stated.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: I voted two, essential. I think it speaks for itself.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I also voted two based on the reasons that were already reported.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential. I appreciate the attention to this issue. I might add that we could include data privacy, which as discussed earlier, the inclusion of HIPPA in a later criterion covers providers and their business associates, but may not cover the sponsors or investigators, so we would want to include that responsibility as part of their purview.

DR. ROSS: Dr. Maddox, how did you

vote?

DR. MADDOX: I voted two, essential. I think data security is nonnegotiable, and I appreciate the prior comment about privacy as well.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: Yeah, I voted two, essential. I think this is absolutely foundational for developing and maintaining trust.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two for all of the reasons articulated by others.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted two, essential, once again for all the reasons articulated by others.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted one, I think it's very important, but I also think it's generally required for any study to get to an IRB, so I don't know if it's necessary to be

included in the CMS requirements.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted one as well. Dr. Whitney said exactly what I was going to say.

DR. ROSS: Dr., or Mr. Kremer, how did you vote?

MR. KREMER: Thanks for almost promoting me. I would associate myself with the comments of Dr. Whitney and Dr. Riddle, but if I were going to vote anything other than zero, but of course I voted zero for reasons stated before, I probably would have voted one. Please do not take that as a vote of one, my vote is zero, but I will also associate myself with the remarks from Dr. Kanter. Good studies are good studies, good study design is good study design, and in endorsing what Dr. Kanter said, I would have liked to have seen this worded a little differently because I think -- well, she articulated it, but we could do better and the way it is worded is not ideal, so that would have also pushed me to one if I were not committed to voting zero.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I would have voted two for optics, because as Dr. Riddle and Dr. Whitney said, these are basic requirements for clinical studies, et cetera, they are required elsewhere, but I think it increases confidence in the data CMS is collecting and will eventually distribute. I think it's important for CMS to check the box.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: So again, my vote, it's a little complex here. I don't exactly concur with the pretext of no existing requirement here. You know, as you heard me mention during the discussion this morning, you know, a portion that we're not voting on is requirement S, where there is this dimension of 45 CFR Part 46 as well as CFR 56, where adequate provisions to protect the privacy of subjects and maintain the confidentiality of the data is in place, and so the no distinct requirement is confusing to me there. I do believe these are important, but it's unclear

to me what this is providing above and beyond the requirement upon which no one is voting today.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted two. I think it's essential to secure data that is being collected, particularly in the course of care for patients, and I think patients would consider that security essential. But I think it's also broad enough that it allows flexibility.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: I would have voted two. I think the only question on that is whether information governance is clearly enough presented to allow an understanding of just what is needed. A data security provision is much more straightforward, I think.

DR. ROSS: Okay, thank you for all your votes. We're going to move to the fourth criteria on which we're voting today. This criteria would encompass two criteria in version 2014 of the CED requirements, the

rationale for the study is well supported by available scientific and medical evidence, and the study results are not anticipated to unjustifiably duplicate existing knowledge. The proposed criteria is, the rationale for the study is supported by scientific evidence and study results are expected to fill the specified knowledge gap and provide evidence of net benefit. Please cast your votes.

(The panel voted and votes were recorded by staff.)

Okay. All votes have been cast. Dr. Drhuva, how did you vote?

DR. DHRUVA: Thank you, sir. I voted a two. I think that these are essential. My only suggestion is that with regards to the specified knowledge gap, sometimes we learn more and sometimes additional knowledge gaps emerge, such as updated technology in long-term data, and I would just like to see that there is still sufficient flexibility if additional knowledge gaps need to be closed.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted two, that this is

essential also. I think it might be strengthened by being specific that it refers to providing evidence of person-centered benefit for Medicare beneficiaries. We talked about net benefit and I think we had a good understanding from Dr. Segal about what that meant, but sometimes people think about benefits to science and benefits to innovation, benefits to other things, and so at least the way I'm thinking about this vote, it's a person-centered benefit.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: I voted two, essential as well. I agree that some better definition of benefits would be valuable since it could be construed as not necessarily just patient centered as was mentioned there.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I voted two, that it is essential. And I also agree that the notion of net benefit could use some additional clarity, and should have a focus on benefits for the patients. So I think that's additional information that may need to be looked at in

terms of defining what net benefit actually is for this particular statement.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential. I think these elements, you know, insure that the study has added value and isn't simply a ritual. I concur with Dr. Fisch's suggestion of stipulating further that it is a net benefit to the Medicare beneficiaries.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted two, essential. I concur with the other comments about clarification of net benefit, and as was brought up in some of the prior discussions, potentially including caregivers or family members could be considered in that.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: Thank you. I voted two as well, essential, on the principle that I believe we need to allocate resources and time and energy and leadership to answering important questions that are about Medicare beneficiary clinical outcomes that are of

substance and consequence. Thank you.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I also voted two and I would just add that I agree that the net benefit needs to be specified to be patient-related outcomes.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted two, essential. I will say briefly that personally and off the record, it is a concern that a broader definition of value is not able to be considered. However, on the record, my vote acknowledges that net benefit is defined in terms of benefit to patients and their caregivers. Should consideration of value ever be included in CMS deliberations, I believe that the goal of net benefit would still be important.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted two, essential. I think that term net benefit speaks for itself, I don't know that it requires any

clarification. And I'm not sure, this question is for CMS, of the extent to which non-member, non-patient, non-beneficiary specific considerations are considered in coverage determinations.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted two as well, essential, and I would echo the comments I believe Dr. Ford made regarding a little bit more clarification around meaning and how CMS was interpreting from this language.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: Have your bingo cards ready, I voted zero again, but I am very grateful to everyone on the panel that particularly highlighted person centered being a critical revision to the text here. We don't have revised text, we have the text before us, I'm voting on the text before us, and I think it leaves dangerous leeway for CMS either now or under a future administration that we may not anticipate, wade into the use of things like qualities, which are inherently in my view

racist, ablest, sexist and you name it ists.

So I don't want to leave that room, and I don't want to vote in 2023 for anything that might be applied down the road taking advantage of the vague language here. So I will join the chorus that's saying this ought to be revised, it hasn't been revised, but it ought to be revised as CMS moves forward to identify that it is person-centered benefit, not any kind of economic analysis or broader societal view of benefit, measuring the needs of some communities against the needs of others.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I would vote two. I think adding something around health outcomes to Medicare beneficiaries is important, I think Doctor -- well, I'm terrible with names, but I think it was mentioned in the discussion that intent was really around health outcomes, not economics.

And I agree with the notion of caregivers and I'm going to leave it up to the lawyers at CMS, because that's a tricky

situation if you've got a technology or service that only benefits caregivers and their family members and they're not Medicare beneficiaries, so I think adding that concept sounds nice but it may be a little bit tricky, but definitely I think adding some reference around net health outcome benefits to Medicare beneficiaries and, you know, leave it to the lawyers about the families and the caregivers.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: I would have voted essential but with the stipulation of consideration of revised wording around net benefit as mentioned from the previous panelists.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted two, essential. I think it retains the important elements of the current CED requirements, that the rationale for the study be supported by scientific evidence and fill a specified gap, which I think is essential.

DR. ROSS: And Dr. Hodes, how would

you have voted?

DR. HODES: I would have voted two, also essential, both on grounds and need, to specify the circumstances in which a study ought to be carried out, but also supportive of further specification in net benefits.

DR. ROSS: Than you, everyone, for your votes. I think we can do one more before our lunch break if that's okay with everybody.

This is the fifth voting item for the day, also related to the theme of context. The original CED requirement from version 2014 stated, the principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of affected beneficiaries who are represented by the enrolled subjects. The proposed criteria, sponsors/investigators establish an evidentiary threshold for the primary outcome so as to demonstrate clinically meaningful differences with sufficient precision. Please vote.

(The panel voted and votes were recorded by staff.)

Thank you, the votes have been cast, Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential, because I think that this is inherently an essential criteria. I interpreted the clinically meaningful differences to mean improvement in clinical health outcomes.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted two, that this is essential also, knowing that clinically meaningful differences are really important. It might be strengthened if there were some way of specifying that it's not just the sponsors and investigators who get to establish that, but it's something that would be negotiated with CMS, that threshold.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: I voted two, essential. I (break in audio) think it's important and it's not looked at.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I also voted two as essential. I would comment, though, on the last couple of words, sufficient precision, and I think that maybe that could use a little bit

more clarification, it could be interpreted differently by different individuals, but I think that the whole concept is essential.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential. Just reiterating the previous panelists' comments, it's clearly a key objective to improve beneficiaries' health, and so we need it to reflect in there clinically meaningful differences. I'm not so firm about, I think we had some discussion around the fact that there's a threshold, we clearly need some minimum standards, and then can work from there.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted essential, but I'll say I voted essential because I think we need someplace to have clinically meaningful differences, and wasn't totally convinced it was in the last one. And I am concerned about the evidentiary threshold and sufficient precision, because I don't know that there's a one size fits all approach for that, it depends

a lot on the patients you're talking about, about the degree to which they have other options, and I would want to be certain that this was not established as a one size fits all across drugs, devices, across all diseases, et cetera. So I don't love the language, but I think having someplace for clinically meaningful differences is important to note.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: Thank you. I voted two, as essential. I consider this an important component of our rigorous methodology.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two. I particularly like the inclusion of evidentiary threshold, and I think it's a legitimate two.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted two for essential. I feel that the evidentiary threshold could or should be motivated by consideration of groups beyond the sponsors and investigators. I agree also that this is quite likely not a one size fits all criterion and

that clinically meaningful differences with sufficient precision are very important.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted two, essential. Like Dr. Maddox, I don't love the language exactly, I think you could strike sponsors/investigators, others may from time to time establish thresholds. I like very much the intent of this, but I do think the wording needs to be worked on a bit.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted two as well. I would call out that clinically meaningful is a very good way of phrasing. I think what we're all trying to get at here, this is not simply a statistical difference in something, but that there is actual meaning to the patients and the caregivers that are subject to the outcome.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: I voted zero so, for context, again, referencing my long statement before the voting began, but also I wanted to

come back to Dr. Maddox's point that this is not workable as a one size fits all and that we need to appreciate the difference between types of items and services. But I would also draw our attention back again to the clinically meaningful phrase, where I think this is insufficiently precise and as a patient advocate I really need the specificity on the record from CMS about what CMS thinks clinically meaningful means.

And here's what I mean by that. There is at least in drugs, maybe devices too, but I know a lot less about devices and services, there's a raging misunderstanding of who gets to define clinically meaningful. If you go back to the researcher that coined the term, he means very clearly patients define what is clinically meaningful to them. But what some are misapplying the term to mean is that clinicians and researchers and government agencies get to define for patients what is clinically meaningful, or should be clinically meaningful to patients. And if this weren't a raging issue, at least in the drugs field, I wouldn't feel any need to draw attention to it.

But it's there, it's real, it's where the rubber meets the road, and if we let anyone other than patients define for them what is clinically meaningful, then this is dangerous. So if that can be resolved through clarification from CMS I'll feel a whole lot more comfortable, and then reduce my concerns to the one size fits all issue that Dr. Maddox articulated.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I would have voted two. I agree with Dr. Maddox and Mr. Kremer around the context matters, and so maybe adding some verbiage to that effect would be helpful. And I agree with Dr. Fisch around the sponsors and investigators, and CMS's role and this, I think, goes back to the comment I made earlier, I think.

Hopefully, CMS will take a look at each of the criteria and clearly articulate who's responsible for what, because if that made any difference, you know, we could read into all the criteria in its totality and say well, all of these are in the protocol, which

may be CMS, but if the protocol is what CMS is approving, then implicitly yes, CMS also approves the evidentiary standard, but it's not entirely clear.

So I would encourage CMS, not only on this criteria but others, just to make sure it's very clear who's responsible for what, and whether CMS is going to play an active role versus looking at, reading the protocol and agreeing that the protocol meets certain standards.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: Yes, so I view it as essential, but when combined with the next question, I know we're not diving into question six yet, but I really don't see how they're evaluated separately. I agree with Mr. Kremer's comments with respect to clinically meaningful differences where definitions in JAMA and otherwise are all over the place. You know, it could be a threshold value pertaining to a change of large or larger as considered meaningful to patients, clinicians or both. A lot of, you know, I

think we've heard consistently about the importance of patient preference and involvement in the design and conduct of these studies, and I think clarity around that definition and clarity around involvement of patient preference information in the design and execution of studies is essential.

And again, not diving too hard into number six, but I think we heard from Dr. Segal on the criteria that, you know, the intent is to have endpoints that would include those that are important to patients and/or clinically meaningful outcomes. And so really putting the patient first in both question five and six is paramount, I think these are essential, but essential with some important considerations around the wording and definitions of these constructs.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted two as well. I couldn't agree more with Dr. Canos, I think it's really important to have an evidentiary threshold to demonstrate outcome differences and to define that up front, but I

do think it's essential to have patients front and center, and I think the next criterion I that we will be speaking about in a moment does that well. So here I might recommend a wording change, something to the effect of to demonstrate outcome differences meaningful to clinicians and patients with sufficient precision or something to that effect, but I do think it's important to have patients front and center when we're talking about meaningful outcome differences.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: I too would have voted two as well. Clinically meaningful differences are clearly an important criterion but I resonate with what we just heard, that maybe modifying that just a bit in the wording to indicate that meaningful to those involved, recipients as well as clinicians, would help to clarify it but no matter what, that's going to be a criterion that's going to be difficult to define and much debated and acted upon case by case.

DR. ROSS: Thank you for all your

votes. So we're going to pause and take a lunch break. We did go five minutes over so we'll extend our lunch break until 12:50 p.m., so it's a half an hour, and when we return we will continue going through the voting questions.

Tara, are there any other announcements before we break? Hearing none --

MS. HALL: I'm sorry, I didn't hear you.

DR. ROSS: Any announcements before we take a break for lunch, we'll come back at 12:50?

MS. HALL: You said 12:45 that we're coming back?

DR. ROSS: I said 12:50 so people have a full half hour, since we went a little bit over.

MS. HALL: Okay.

DR. ROSS: Okay, see everyone in half an hour.

(Lunch recess.)

DR. ROSS: Welcome back. We'll give people a moment to get back and to turn on their cameras.

Great, well, welcome back to everybody after lunch, we're going to pick up just where we left off.

The next voting question in front of us is also within the theme of outcomes. There was no existing requirement in the 2014 version of the CED requirements. The proposed criteria is, the primary outcomes for the study are clinically meaningful and important to patients. A surrogate outcome that reliably predicts these outcomes may be appropriate for some questions. Please vote.

(The panel voted and votes were recorded by staff.)

Waiting on two more votes. Is there anyone who is trying to vote and hasn't been able to? Let's see if we can figure out the discrepancy by going around. It looks like we're one vote short of what I anticipated, an N of 12. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential. I think that these are essential requirements. I think that, a couple comments to make. I think that these clinically meaningful endpoints should consider patient symptom

burden, quality of life and functional status, but I think with the line regarding surrogate outcomes, I think that reliably predicts should really be a validated surrogate endpoint.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted a two, essential. I'll just observe that this time the reference to clinically meaningful didn't really refer to sponsors/investigators so I like this more generic phrasing of it compared to the prior question. I think it could be strengthened by maybe being more specific about what we mean by to patients, right, so we're not talking about patients with a condition worldwide or across all age groups, but we're talking about Medicare beneficiaries, and I think patients doesn't necessarily have to be completely limited to the subset of those affected by a given condition, so utility or some other measure of preferences could get more broad than just the very very narrow set of let's say individuals affected by a rare disease and how they view the world.

DR. ROSS: Dr. Flannery, how did you

vote?

DR. FLANNERY: I voted two, essential. I'm not a fan or surrogate outcome measures; however, in light of item five, where we have every (break in audio) the occasion in the surrogate outcome could be used.

DR. ROSS: Dr. Ford, how did you vote? Dr. Ford, you're on mute.

DR. FORD: Sorry about that. I also voted two, essential. I would echo the comment about consider changing patients to Medicare beneficiaries to be more specific for this population.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential. I do think it's an important complement to criterion D with its focus on patients. I might remove the surrogate outcome mentioned, not sure of the need for that at the outset.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted two, essential, and don't have anything to add more than the prior comments.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: I voted two, essential. I think it's a patient-centered requirement. I also like that it acknowledges that we need to be cautious with surrogate or intermediate outcomes, but the earlier points made, that if they are validated, we know there is a direct correlation, I think it makes sense. Thanks.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two. I think the statement regarding surrogate outcomes being reliable predictors is appropriate.

DR. ROSS: I notice Dr. Stearns came off. Is Dr. Stearns back? I wonder if she's have Internet trouble. CMS team, can you just let me know when she comes back?

MS. HALL: Yeah, we will do that.

DR. ROSS: Thank you. Dr. Whitney, how did you vote?

DR. WHITNEY: I voted two, essential. I agree with the prior comments, particularly around the need for surrogate outcomes to be demonstrated to accurately predict the outcome of interest.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted one. I think this is important although I'm a little bit confused as to whether this statement and the previous statement that we discussed before lunch somehow could make it actually more ambivalent as opposed to clarify in outcomes. Honestly, I know we're not word-smithing, but I would just strike the first sentence and somehow incorporate into the previous statement and then speak to how we wish to examine surrogate outcomes if appropriate for the question or the issue at hand.

DR. ROSS: Okay. Mr. Kremer, how did you vote?

MR. KREMER: I voted zero. So, again, the explanation I gave in an overarching sense. I'll just say I feel better about this one than I do some of the others. I very much appreciate the explicit reference here to the person-centered point of view and patient preference, which we all understand is enshrined in statute, among other places things like 21st Century Cures. The focus of the

federal government as congressionally legislated and signed by the President is on person centeredness and patient preference, and I appreciate this highlighting that, magnifying it, emphasizing it, choose your descriptor, in a way that maybe some of the other voting questions don't, and I do think it's important to retain a reference in any good clinical study design to the importance of surrogate outcomes.

I will just close with this, and apologies if I've forgotten an earlier part of our two-day meeting. I'm a little lost as to why we need the and important reference if it's meaningful, but I'm not trying to engage in debate, just noting for the record that I don't recall an explanation of why we needed that additional couple of words.

DR. ROSS: Thank you. But before I turn to the nonvoting members, Dr. Stearns, I know you had Internet trouble and you're back on. How did you vote?

DR. STEARNS: I'm back on. I'm not positive my vote has registered by the numbers you've got there, or has it? But I voted two,

and I did have a brief comment on this. I'm sorry because my Internet went out and I missed some of the things that other people have said.

My comment actually comes from one of the comments that was sent to CMS specifically from the Schaffer Center and with respect to thinking about a surrogate outcome. The point that I want to make is that outcomes should be of high importance to the targeted patient populations and their caregivers based on quantitative evidence of the risks and benefits, so I would add that comment, and sorry for the Internet.

DR. ROSS: That's no problem and actually after we conclude discussion of our votes, we're going to confirm whose vote did not count, so we'll have to pause for a moment to figure that out.

But in the meantime, Mr. Patel, how would you have voted?

MR. PATEL: I would have voted two. I agree with Dr. Riddle, maybe combining the concept of clinically meaningful and important to patients could be done in the criteria. I would leave surrogate outcomes because frankly

if you take it out, it causes kind of an absence in the future of any measure where surrogate outcomes could apply, that it's not allowed here. You certainly want to make sure that the surrogate outcomes are validated, of course, I think that's what reliably was trying to get at, but if we want to add some more caveats, there are more different outcomes, I think that's a good idea.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: I would have voted two, essential. I concur with Dr. Dhruva on the need for them to be validated surrogate outcomes and I also agree with Dr. Riddle for that type C, that requirements five six should be linked for clarity.

And to Mr. Kremer's point, you know, and as I stated before lunch, when seeking clarity from Dr. Segal on intent of both important to patients and clinically meaningful, I asked about the union of events versus the intersection, and she said both would be an important outcome to be included. You know, I would propose a change of wording

here where we would put the patients first. I would say the primary outcomes of the study are, one, important to patients, and/or two, clinically meaningful, and then from there having the surrogate, validated surrogate outcomes described with the possibility of combining with number five where we talk about precision and needs for precision.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: Two, essential. I like the focus on outcomes that are important to patients and I think the statement gives flexibility around surrogate outcomes. I think it's nice as written.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: I would have voted two. I'm in agreement with both meaningful and important. The patient-centered clinically meaningful outcome aspect and leaving flexibility for surrogates as appropriate, I think is also important.

DR. ROSS: Great, thank you all for voting. Tara, let us know when you have been

able to figure out which committee member's vote did not register.

DR. STEARNS: By the way, I logged out and logged back in to the voting site and it doesn't seem to want to register my vote.

DR. ROSS: I think we have a culprit, Dr. Stearns.

DR. STEARNS: Yes, sorry, so I suspect I'm the one. I'm hoping when the next vote is taken, it works again.

MS. JENSEN: Yes, it's not going to be a problem. We can see it in the back end, it will be on the transcript and we will hand write it in for the score, so no worries.

DR. ROSS: So Tamara, I should expect only 11 votes going forward, just to confirm?

MS. JENSEN: We'll see if we can work behind the scenes to get her locked back in, but if we can't, it's not a problem.

DR. ROSS: Okay, thank you.

So we'll turn to the next voting question, which relates to the theme of protocol. This incorporates two prior CED requirements, the study has a written protocol that clearly demonstrates adherence to the

standards listed here as Medicare requirements, and the clinical research studies and registries are registered on the www.clinicaltrials.gov website by the principal sponsor/investigator prior to enrollment of the first study subject. Registries are also registered in Agency for Healthcare Quality's Registry of Patient Registries.

This has now been modified to the proposed criteria of, the CED study is registered with clinicaltrials.gov and a complete protocol is delivered to CMS.

Can we bring the votes back up? Oh, sorry.

MR. KREMER: Joe, can I interrupt briefly on a technical matter? We didn't see that on the screen, on the webinar screen the way we had the previous ones, and my voting screen has not advanced to that question.

DR. ROSS: Tara, can you pull up the voting screen?

DR. WHITNEY: Same here.

DR. OGUNWOBI: Same for me.

DR. ROSS: So you all are just seeing each even other, it did not share the screen

then.

MS. JENSEN: All right, I'm working behind the scenes, we're getting it up if you'll give us one minute. Sorry.

DR. ROSS: No problem.

MR. KREMER: Thanks, Tamara.

DR. OGUNWOBI: The voting website is shill just showing outcome six.

DR. ROSS: Okay. We'll see, something may have paused it.

MS. JENSEN: Yeah, maybe us pulling it off may have delayed it, so give us 30 seconds just to see.

MR. PATEL: Actually, can I go back to the last one and change my vote to three instead of two, because that was probably the most important criteria from my perspective so I should have voted three on that one.

DR. ROSS: Mr. Patel, that was not a choice.

DR. MORA: Dr. Ross, we're holding you personally accountable for the technical difficulties as well.

DR. ROSS: No, I know. That's part and parcel of our code, but look, I fixed it.

Okay. We're moving to question number seven. Okay, great.

So I won't reread the prior criteria but the proposed criterion is, the CED study is registered with clinicaltrials.gov and a complete protocol is delivered to CMS. Please vote.

(The panel voted and votes were recorded by staff.)

All right, 12 votes, so that means everyone's voting is working. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential. I think that registration at clinicaltrials.gov is essential. I'd also add, I think that it's important that if there are any updates to protocols, which occurs commonly for a variety of reasons, that these are also updated in a timely manner.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted that this is essential, I voted two. I agree with Dr. Dhruva that updates should be done as well in a timely manner. I also believe that I

would go one step further, I would strengthen this by requesting redacted protocols to be publicly available, particularly at the time of protocol activation. Just like journals often have a supplementary appendix with protocol when studies are published, they can be redacted to get rid of proprietary information that sponsors don't think are appropriate in the public sphere, but I think this additional step would be very useful.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: I voted two, essential as well (break in audio) previous comments it looks like.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I voted two as well. I agree with the previous comments, I'll leave it at that, I agree with the previous comments.

DR. ROSS: Okay. Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential. Registration is key for accountability. I might include some investigation of what it means to be complete, but that could be done

elsewhere.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted one, important, although that's partly, I think, due to my -- these things are in somewhat of a strange order, I would argue, and so I had actually thought some of this was included in the prior elements around requiring a written plan, a protocol with information, governance and data security provisions, et cetera, et cetera. So I guess my only comment would be that all these things could be combined somewhere in terms of protocol, but I do think it's important that things be appropriately registered and delivered to CMS. I just thought it was a bit redundant to have them all on separate lines.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: I voted one, it's important but not essential.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two for the reasons that were previously stated.

DR. ROSS: Dr. Stearns, how did you

vote?

DR. STEARNS: I voted two. I would emphasize that updating the protocols should be done in a timely manner, and I would agree about the consolidation possible across criteria.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted two, essential. I think another advantage of requiring the clinicaltrials.gov registration is the publication bias constructs which we talked about, so when studies never get past the registration phase, it suggests there may not be the results they were expecting.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted one, that this is important and not necessarily essential as written. I think having the protocol delivered to CMS is a nice first step, but I agree very much with Dr. Fisch's comments earlier about that protocol being appropriately redacted when necessary, but available for public consumption as well.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: I voted zero and will just say, big fan of clinicaltrials.gov, I think probably most of us are, and will associate myself with the comments about redacting and about modifying the protocols.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I would vote two. I think making sure that the appropriate redaction is there but also as mentioned in the discussion, giving CMS an updated protocol if there were protocol changes that were made or some discussion about how that would occur, I think is also important to add in here.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: I would have voted two. I believe it's mandatory to report to clinicaltrials.gov NCT numbers on Medicare claims for services that are provided in clinical research studies that are qualified for coverage, so as I read this I don't think it's optional, so I think they need to have a

clinical trials history to actually from, so maybe folks can prove me wrong there, but the part that I see us discussing is the protocol, and I think that's essential, that the protocol go to CMS.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted two, essential. I very much agree with John Whitney's comments earlier about the importance of registering trials, particularly to understand the existence of publication bias. I would also add the caveat, the prior requirement stated when the protocol should be posted prior to the enrollment of the first study subject and I don't see that here, so I don't know if this should be amended to include a specific time or not.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: I would have voted two, essential, and would also enforce the suggestion when we had comments about the updates to protocols when they occur.

DR. ROSS: Thank you for your votes.

Just a note, that we discovered whose committee member's vote was missing for the last question and it was actually Dr. Dhruva. His vote was captured verbally for question six and will be included in the record so everyone is aware.

We're going to move on to the next voting question, this relates to the theme of population where there was no existing criteria before. The proposed criterion is, the study population reelects the demographic and clinical diversity among the Medicare beneficiaries who are the intended users of the intervention. This includes attention to the intended users' racial and ethnic backgrounds, gender and socioeconomic status at a minimum. Please cast your votes.

(The panel voted and votes were recorded by staff.)

Okay, all the votes have been cast. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential. I think it's essential that this criterion be added. We often lack this information and there's oftentimes variation in benefits and

harms based on the variety of factors listed here. It's absolutely essential that this be added.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted two, that it is essential, and I like the way it's written, I don't have any further comments.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: I voted two, essential. I'm not certain we need at a minimum, it could just state these but nothing else.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I voted two, essential. I would change some of the wording around. I think that somewhere it needs to include a representative sample size of, representative sample size of the intended users' racial and ethnic background, gender and socioeconomic status. I think that there should be some type of required, requirement to include enough of a particular population that is being studied to have effective and accurate data.

DR. ROSS: Dr. Kanter, how did you

vote?

DR. KANTER: I voted two, essential. I think this is an entirely appropriate criterion for the reasonable and necessary statutory standard for CMS, and really appreciate the sentiment. I would note that as we discussed, socioeconomic status is not a standard element in claims data, it's very difficult to actually obtain that on an individual level, people sometimes won't tell you even if you ask them, so I'll just put that in for the record.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted two, essential, and while I recognize it can't go into this verbiage here, I would very much encourage CMS to lead on helping to develop criteria and a standard approach to how this could be implemented, because I think it should be. This has the potential to resonate far more broadly if done well, so this is an opportunity to really elevate the importance of this particular principle.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: Thank you. I voted two as well. I echo Dr. Maddox' comments, I think this is a big ground and an important point. Thanks.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I also voted two and I agree with the comment made by Dr. Ford, and I believe Dr. Maddox, you know, the sample size should be representative and adequately powered to include all of these diverse groups, and the goal should be to diminish health disparities as far as given health outcomes.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted two, essential, and I agree in particular with the comments by Dr. Ford and some others. The comment that I will add is that the word intended possibly could be considered, regarding whether sample sizes should be sufficient for certain subgroup analyses, which is a little different than having a representative population necessarily.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: Two, essential. I agree particularly with Dr. Maddox's comments about the potential benefits of this being launched well. I do think there's a problem with the phrase users of the intervention; that's not really Medicare ese, I think maybe recipient of the service, because you're not looking at the interventions in the sort of omni lexicon of what an intervention might be.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted two, essential as well, and echo the comment I believe made by Dr. Maddox about how this has far reaching potential beyond just this reporting requirement.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: It breaks my heart that I voted zero on this one. I feel as strongly as I think anyone else on this panel about the importance of the concept here, but I have deep reservations about how CMS will utilize this kind of requirement based on the experience that we've seen with how it has been utilized

in the case of the community that I represent in particular through my day-to-day work in Alzheimer's and related forms of dementia. This is an ideal, but how it gets implemented is where the rubber meets the road for affected communities, particularly communities that are disproportionately affected by conditions like but not limited to Alzheimer's disease, and if this is used counter to its real intent by us as a way to limit access for communities that face the highest burden of disease based on these sort of demographic considerations, then it will be counter to our purpose in endorsing this in our advisory role.

And I'll just give a last point as an example. If this weren't in the CMS context, if this were just about how studies ought to be designed and what standards they had to be held to generally, not in a CMS context, in a CED context in particular, this doesn't go nearly far enough. And the concrete example I'll give you again particular to my work experience, but probably more broadly applicable is the Down syndrome and intellectual disabilities communities who are routinely excluded from

clinical trials for Alzheimer's disease, therapies, diagnostics, et cetera. And yet, they face the highest rates of Alzheimer's of all communities; African Americans are twice as likely as Caucasians to have Alzheimer's, but something like, depending on which studies you look at, 50 to 90 percent of people with Down syndrome who reach Medicare beneficiary eligibility will have Alzheimer's disease, and yet they're excluded from the trials. So I don't know that even with the phrase at a minimum, I don't know that this goes far enough, so I think it could be strengthened, and I appreciate and endorse the concept and the priority that we all want to put on this, but I have to vote zero again given my contextual concerns about CMS's authority and operationalization of these requirements.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I would vote two. I agree with everybody's thoughts around the importance of this. I agree with Dr. Kanter's caveat for, about the difficulty of collecting some of this information, not only socioeconomic stuff but

I'll use the racial and ethnic to the extent that patients opt not to provide that information, so I think we have to recognize that.

I do agree with what Dr. Whitney said. When I read intended users in both sentences, it struck me as odd, and then I would think we could simple replace users with patients, or Medicare beneficiaries, in both sentences, because I really do believe that was intended, that was the rationale behind it, and not the outliers that might be using the technology to deliver the service.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: I would have voted, well, one as important. I agree with Dr. Maddox's statements. I do share Mr. Kremer's concern regarding unintended consequences of this, and kind of reflecting back to the race to the perfect study that has full ascertainment for the diverse population of Medicare. I think it's important, very important to have that study be reflective of the population, but I want to kind of consider the data collection

related to these CEDs balanced out to provider burden, understanding that not, you know, that the rural providers don't have the same data collection, clinical data efforts, collection efforts, research sciences that some of these academic research centers do, and many times the data collection efforts fall on the provider, and would not want this to become a criterion that results in inadvertently creates a barrier to access to care.

I think we heard from Dr. Bach Bockstedt about some tiered approaches to data collection where there's a, you know, a more clinically rich deeper dive than a traditional study context, but then having a wider base on claims looking for adverse events. You know, if this were to go forth, I would encourage, you know, be supportive of Medicare working with individuals to insure it does not become a barrier to care, and that it's, you know, where appropriate kind of leverages existing methodologies used for data collection that reduces the provider burden for data capture and where appropriate, aligns with the existing requirements for that part of the study.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted two. I think it's essential, I think it's a critically new requirement. I greatly appreciate, I think the first sentence of this two-sentence requirement, I think captures it really well. I do worry somewhat about the second sentence and how specification might have unintended consequences, as has been mentioned by a number of the panelists, in particular the practicality of collecting some of this data like socioeconomic status at the individual level.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: I would have voted a two, essential. I think it is a new and critical element that's attending to an important aspect. I think the notion that attention be paid to intended users or beneficiaries leaves the kind of flexibility that we, many of us agree is important, and just what degree of data and diversity and initial approval versus subsequent monitoring is going to be an optimal

solution in a given case.

DR. ROSS: Thank you for your votes. We're going to move on to the ninth criteria. This relates to the theme of generalizability. The prior criteria was, the study protocol explicitly discusses how the results are or are not expected to be generalizable to the affected beneficiary subpopulations. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

The newly proposed criteria is, when feasible and appropriate to answering the CED question, data for the study should come from beneficiaries in their usual sites of care, although randomization to receive the product may be in place. Please cast your votes.

(The panel voted and votes were recorded by staff.)

We seem to be a vote short, if everyone would confirm that very voted?

MS. HALL: Can everyone just vote again to make sure the system it capturing the votes?

DR. ROSS: Okay, that's 12 votes,

hopefully we got everybody's vote correctly, and we'll be able to confirm through public statement. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential. I think we certainly need to have data from a beneficiary's usual site of care. As discussed in my question to Dr. Segal yesterday, the word although need not necessarily be there. If we think about rigor of evidence generation, we know that randomization when appropriate provides the greatest rigor of evidence generation, and as we currently strengthen our evidence generation system in the United States to conduct trials with more pragmatic elements, certainly randomization at point of care where patients are getting their usual sites, where patients are at their usual sites of care is increasingly feasible.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted one, that this is important. And I think could be strengthened just by removing the clause about although randomization to receive the product in place; it's just awkward.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: I voted two, essential. I agree with the issue about the randomization statement.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I voted one. I think it is important and I have the same concern about the randomization clause.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted one, important. There are three concerns I had.

One is the purpose of the randomization phrase at the end. Second, I think there was some meaning that was lost from the existing requirement to the current requirement which really doesn't capture this notion of generalizability. Thirdly, usual sites of care although nice, I think that there are other ways to generalize from the study to the Medicare population, and I would be okay with that.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted on, important. I agree with Dr. Kanter that the concept of generalizability may have gotten to a more important piece in number eight than in this, and I don't really understand why usual sites of care enhances generalizability necessarily. Usual site of care can mean something very different if you're receiving a very unusual device that needs high tech training versus if you're receiving, you know, sort of a standard medication that you can get from a primary office, and so I'm just not sure I see the necessity of this element, given that we have in a prior one, it talks about being inclusive in the way that these studies are conducted.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: I voted one, important. I don't have anything to add to the prior comments. Thanks.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two because I thought it was helpful to a lot of flexibility of, you know, this data being able to be collected in usual sites of care for us when

opportunities for randomization are possible.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted one. I believe this is important but not essential, this aspect of generalizability. I also have a specific wording suggested change, which is that the phrase, the last phrase be changed to although randomization to receive the product may, and then change it to may shift the site of care in some cases. So that's my suggestion.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted zero, not important. I think the requirement as written is essentially unenforceable, it's vague, it has so many, you know, feasible and appropriate caveats that it would make it not able to be used, and I think the study sponsor has a clear interest in making sure they have generalizable data. So depending on the specific service, you know, if it's highly specialized, it won't be in, quote, their usual site of care, because it will be happening in some tertiary site or

institution, so think this is not needed. Thank you.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted one, important. I echo the comments Dr. Whitney made.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: With no surprise to anyone, a zero. I'm delighted even though his rationale is different, I'm no longer alone and Dr. Whitney also voted zero. I will just register for the more important element than voting is the discussion, that I have concerns about the reference to usual sites of care and the reference to randomization, based on how CMS might in the real world apply those terms.

Usual sites of care can be misapplied in order to restrict access and threaten the health equity concerns that we all spoke to on the preceding questions. So there are, as some or perhaps all of you know, extraordinary shortages of specialists in certain fields, and that has relevance for what is currently or what in the future may become the usual sites

of care, and so I think there is an opportunity for misuse of that otherwise laudable notion.

Randomization, I don't know anyone that doesn't value RCTs, but there's a time and a place, and for me the time and place is an FDA matter in Phases I through III, and really obviously Phase III, and where FDA requires it, a Phase IV study. I have deep concerns about anything that might lead to a requirement of an RCT for a postmarket coverage decision, particularly where RCTs can have a variety of negative consequences, not all of which I'll articulate, some of which were articulated in the public comments that we received in writing, and I believe were also spoken to, but among other things, they can also affect equitable access, health equity access, particularly for traditionally minoritized populations.

So there is danger here from my point of view across disease states and across population groups to anything that might imply authorization for further use of, further insistence by CMS on use of RCTs, either for an accelerated approval product or traditional

approval products.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I probably would have voted a one. I think this is the criteria I had the most difficulty with. The term usual sites of care, I think in the past discussion referred to sites of care such as outpatient hospital, et cetera. And when you say usual sites of care, is that a current usual site of care that's expected, or maybe the expected site of care might be even more appropriate, particularly as you see services go from inpatient to outpatient, from even a facility, a hospital, a clinic, to a home study site. That troubles me, what is meant by that, and what would be expected, frankly, of a sponsor in terms of what's expected in that.

And then the second piece, the awkwardness of, although randomization is a bit awkward, I'm not quite sure what they -- I think I know what they mean, and it may not be possible to do this because of randomization and maybe that's what the was, but I think that needs to be clarified, because I am, I would be

troubled if the notion is randomization is required to do that.

And then a third piece, really, to receive the product, I really think that focuses in on particular devices and it may be better and probably should be, to say receive the services regardless of what we say about the kind of randomization, because a CED could also be applied to services as well. So I would eliminate the word product and replace it with services, realizing this is CMS's language.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: I would have voted one, important as well. I concur with other statements about dropping kind of the caveat of although randomization to receive the product may be in place.

Going back to the charge for this MEDCAC, or the issue as stated on that, you know, we're looking at the purpose as driven by topic in question and health outcome studies, an making sure populations of the study is representative. And it provided an example in

the charge that some questions may be sufficiently answered through analysis of other evidence, including a data registry, through VHRs and administrative claims. If the intent of this wording gets at, you know, really thinking about pragmatic studies, leveraging healthcare accounting data, or secondary data that's selected by an entity for another purpose, you know, EHR, administrative claims, then you know, I'm on board with the language, it makes sense, it's consistent with the charge and where appropriate the methodology should be leveraged.

But with the wording as it currently states, I do share concerns the rest of the panel has on the beneficiary data and their usual sites of care as mentioned here. But if the intent, again, if the intent is on the pragmatic trial aspect of studies, I would certainly be supportive of revised wording that gets it more to the heart of that.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted one. I think this is important. I particularly

appreciate the spirit here of increasing access to services at usual sites of care and the generalizability of information that would I come from that. I do worry, though, about misinterpretation of usual sites of care, and this initial clause, when feasible and appropriate, for answering the question is really important. Obviously some services can be provided at usual sites of care; other highly technical services, as folks have shared, tertiary coordinated centers may be the safest place to provide those services. So I think it's important but not essential.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: I would have voted one, important, and particularly would reinforce what Dr. Umscheid has said. Feasible and appropriate is useful in getting flexibility; on the other hand, it's incredibly difficult, subjective and problematic for that reason.

DR. ROSS: Thank you for your votes. We're going to turn to item number ten, dealing with data quality, for which there was no existing requirement in the 2014 version of the

CED requirements. The proposed criteria is now, the data are generated or selected with attention to completeness, accuracy, sufficiency or duration of observation to demonstrate durability of results, and sufficiency of sample size as required by the question. Please cast your votes.

(The panel voted and votes were recorded by staff.)

Okay, all of the votes are in. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential. I think all of these components are very important, or sorry, I should say essential. I specifically want to focus on the durability. We oftentimes learn about particular safety risks that may take time to emerge, and I think it's very important that we see, that we have language about duration of observation and demonstration of durability.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted two, essential, and I agree with Dr. Dhruva's comments.

DR. ROSS: Dr. Flannery, how did you

vote?

DR. FLANNERY: I voted two, essential, and I agree with the previous comments.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I voted two as essential. However, I do have a different opinion about durability. I think it can mean different things to different groups, so I would consider another possibility. I know that we discussed that yesterday, but I'm still not a hundred percent on the use of the word durability.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential. These are all desirable features of data to have in a credible study. I would also add that we might want to change the phrase durability of results; do we mean durability of net benefits observed, just to get some more precision on that.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted two, essential. I think this concept is essential. I have concerns about some of the language in it. I

think timeliness needs to be added per my prior comment about how to ensure that the data are collected in an early and often fashion.

I would love to find some way to indicate community input or patient input into sort of deciding about what elements are important, maybe that goes in the outcomes section and not here, but I forgot to bring it up then so I'm bringing it up now.

I also wrote down that I didn't like the term durability for the same reason. I don't know that we are necessarily only looking for durability of results. There could be different results that are later and not early, and therefore not at all durable but just don't show up until later, so I think it needs to indicate that we want short-term and long-term results over some appropriate timeframe for the intervention being considered. I don't think the term durability actually captures that.

And this is, sorry, also not quite here, but I kept thinking there was going to be something about safety being an important component of the net benefit of the things that we looked at, and I don't know if that goes

here or if that's just saying something about the, maybe that's the completeness of the outcome ascertainment or something like that, but that cued to me too, it's not the durability, it's the short- and long-term effects, including safety, which then made me think maybe I should have brought that up earlier along with community involvement in this selection.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: I voted two, essential. I think this requirement is consistent with a rigorous methodology. Thanks.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two, and I actually agree with Dr. Maddox's comments.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I vote two. I want to reiterate the importance that Dr. Maddox commented, and based on the discussion yesterday, I would change the beginning sentence to say the data are generated or the data sources selected, to avoid any concern

about other types of selection that would not be desirable.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted two, essential. I think, I appreciate the prior comments. I do think duration is, and durability are really important constructs here. Thank you.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted two, essential. I would echo Dr. Ford's comments about what exactly we mean here with durability.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: Again, I would have loved to have voted two and I voted zero. I share the concerns of Dr. Maddox in particular about durability. I only feel, add a little caution about getting into safety and efficacy considerations that are, again, overtly FDA's domain and overtly not CMS's domain. But part of my concern about the durability issue and however that ultimately may get rephrased by CMS down the line, is hoping there will be some

direct reference in this question in relation to durability to the patient preference and person-centered point of view on what durability means.

And this really relates very centrally to my repeated earlier points about how a one size fits all approach is not only problematic but potentially disastrous for a number of patient populations. Durability of results for a short field like oncology almost certainly are fundamentally different than for a relatively young field generally, and in particular for disease-modified therapies like Alzheimer's disease. We aren't going to have, probably in my life, I hope I'm wrong, we aren't likely to have anything that any of us would call a cure for Alzheimer's --

DR. ROSS: Mr. Kremer, I'm sorry to interrupt, but I do not want to talk about specific therapies, we are talking about the criteria.

MR. KREMER: I'm only using it as hopefully an illustrative point, I'm not trying to make this about one disease, it's just the one I know better than others, but, so I'll

rescind the reference to Alzheimer's, I'll just say durability is in the eyes of the beholder, the beholder is the patient, it's not the clinician, it's not the researcher, it's not the study sponsor, and God help us, it's not a federal agency, no matter how benevolent and well intentioned the individuals in that federal agency may be.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I would have voted two and as I mentioned yesterday, I think it would be helpful to separate data sources that are selected and data generated in that first sentence to make it very clear. And I think if you were very explicit about this is all about the sources of the data and look at it generally, I think the safety element is actually addressed in criteria L, from my perspective, because I do agree the data for the study has to be connected, and I think L covers that.

I also have similar concerns around durability, it can mean many things to many different folks. I think what they're trying

to get at as somebody touched on earlier, short-term and long-term outcomes. If that's the intent, a wording change I think would be helpful. But in any case, I also think it's important to add the caveat important before that because again, we don't want to have situations where one size fits all, so appropriate I think depending on the context of the technology, of the service, to try to make sure that word is in there when we're talking about long-term and short-term outcomes, if indeed that's the intent.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: So, good question. So, I view this as important. I'm a little conflicted on the vote here. I find data quality to be a complete misnomer for this mixed bag of statements. You know, sample size in and of itself is not data quality. Within the design aspects of the studies in CED we already talked about threshold, we talked about precision, and so I would inherently, I don't think data quality is that, it's a design aspect or study aspect.

I do also share concerns on the use of the word durability as it pertains to duration of effect. You know, primary outcomes are explicitly called out within the study design aspects where an outcome should be assessed at a certain period of time. I'm not sure how durability factors in here in data quality when it's already covered elsewhere within requirements.

I find big portions of this to be duplicative of other areas. If this element was in and of itself about data quality and completeness, I'd say absolutely essential, but I find many of these elements to be already covered.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I completely agree. I think as written, I would say one, this is important, but I do think a lot of these concepts as Dr. Canos was saying, are captured in other criteria, particularly sufficiency of duration of observation, I do think that is captured in developing the primary outcome of the study. I think sufficiency of sample size

is already addressed in criteria D around necessary precision.

So I agree, I think data quality, accuracy, completeness is essential, but as written, I think this is important.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: I also would have voted important, one, not because these aren't all critically essential dimensions, but I think they are redundant to other of the elements we've discussed.

DR. ROSS: Thank you for your votes. We're going to move on to question number 11, or criteria number 11 for which there was no existent requirement. The proposed criteria is, sponsors/investigators provide information about the validity of the primary exposure and outcome measures, including when using primary data that is collected for the study and when using existing, in parentheses, secondary data. Please cast your votes.

(The panel voted and votes were recorded by staff.)

Okay, all the votes have been cast.

Just a reminder to please keep your comments as concise as possible. We still have a ways to go and only about an hour left in the allotted meeting time. If you're echoing or reinforcing comments made by others, please just be concise in saying that.

Dr. Dhruva, how did you vote?

DR. DHRUVA: Thanks. I voted two, essential. A couple of comments, because I think the validity of exposure can be difficult, particularly for medical devices that are hard to track without a unique device identifier or at least a device identifier in claims data and electronic health records.

The other comment I'll make is secondary data or real-world data, they require validation. These data are generally collected during routine clinical care, and there's a lot of work that needs to be done so these can be used for reliable causal inference about benefits and harms to Medicare beneficiaries.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted a two, essential. I found this confusing, I did a little bit

better when I looked at Dr. Segal's slide 35, item K, which we really emphasized that this is in the context of secondary data, it made more sense to me. But the bottom line is if you want to make a judgment about how the exposure to a service is related to an outcome, you have to have a valid measure of the exposure and a valid measure of the outcome, so it's essential.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: Two, essential.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I voted two, essential, and I echo the comments that were made.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential. Certainly having valid measures is important to having valid outcomes and I think it is, I mean, I think the key here is it's incumbent on sponsors and investigators to justify their selection of these measures.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted a one, important. It just felt a little overly proscriptive to me, and felt like something that would be done as a part of a study anyhow.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: I voted two, essential, and agree with Dr. Dhruva's comments.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two, and I agree with Dr. Kanter's comments.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted two, essential, and I suggest for clarity based on the discussion yesterday, that the word exposure be rephrased with exposure to treatment or service.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted one, important, and I would echo what Dr. Maddox said.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I also voted one, that it

was important, and similar comments to Drs. Maddox and Whitney.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: I voted zero, and again agree with Dr. Maddox on the substance.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I would have voted one. I agree with Dr. Maddox, I mean, some of these can be combined with other elements as well, so I'm not sure it's necessary.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: One as well. As stated before, or as Mr. Patel just referenced, with the addition of, I'm not exactly holding the necessary distinction of existing, that adjective before secondary, whether it be prospective or retrospective, you know, intent or, you know, going forth with secondary data, validity would be important for primary or secondary data without the need for the adjective before secondary.

DR. ROSS: Dr. Umscheid, how would you

have voted?

DR. UMSCHEID: I would have voted two. I think this is essential for a good study design like Dr. Kanter said.

DR. ROSS: And Dr. Hodes, how would you have voted?

DR. HODES: I would have voted two, essential, with a suggestion of clarification of primary exposure.

DR. ROSS: Thank you for your votes.

Okay, we are moving to item number 12, design. I just want to confirm, there are two items here. CMS, should we be ment voting on each separately, correct, two bullet points? That's how I had planned to do it. Tamara, can you confirm, or Tara?

MS. JENSEN: Sorry, something just happened to our screen where it went blank. Can you repeat? We were looking at a blank screen here. Can you repeat the question, I'm sorry?

DR. ROSS: Sure. In the next session, on the screen are the two old criteria and actually two newly proposed criteria, and I was going to ask the members of the committee to

vote on them separately. Was that your idea or did you want me to have both criteria be voted on at the same time?

MS. JENSEN: I think they're supposed to be voted on at the same time.

DR. ROSS: Okay.

MS. JENSEN: I think that's how the TA came to us, so yeah.

DR. ROSS: Okay.

MS. JENSEN: I can understand why that -- yeah, that's probably easiest.

DR. ROSS: So this relates to the theme of design in both prior criteria, where the study design is methodologically appropriate, and the anticipated number of enrolled subjects is sufficient to answer the research questions being asked in the NCD. As well as, all aspects of the study are conducted according to appropriate standards of scientific integrity.

The proposed revised criteria are, the study design is selected to generate valid evidence safely and efficiently for decision making by CMS. If a contemporaneous comparison group is not included, this choice must be

justified. And, the sponsors/investigators minimize the impact of confounding and biases on inferences with rigorous design and appropriate statistical techniques. So please cast your votes.

(The panel voted and votes were recorded by staff.)

We need one more vote. There we go. I would ask when you explain your vote and you rationale, if you could to make it easier for CMS, please make sure you reference whether you're referring to the first bullet or the second bullet for any suggestions.

Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential. To the first bullet, I think studies are certainly strongest when they have active controls, so I think it's important that there's justification of why a comparison group may not be included.

And to the second point, I think that as we see, I think it's incredibly important regarding minimizing confounding and bias, and when appropriate, randomization is actually the most rigorous way to minimize confounding and

bias, and is the most rigorous design when there's not evidence of benefits and harms to Medicare beneficiaries.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted two for the first and two also for the second part of this. I only point out that, Dr. Ross, when you spoke about the first one you talked about the choice may be justified, but the wording is must be justified, and I agree with the must be justified wording.

DR. ROSS: Oh, Freudian slip. I was editing in my head.

Dr. Flannery, how did you vote?

DR. FLANNERY: I voted two, essential for both.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I voted two for the first bullet and two for the second bullet. However, for the first bullet, some of this information has been stated in previous areas like, you know, adequate protocol, et cetera, so I'm wondering if certain parts could be reduced so that we don't repeat the same information in

different parts of the protocol.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential. One comment I would make is regarding the first bullet point. I would strengthen it more. So currently the choice of not having a contemporaneous comparison group is just must be justified. I can think of a number of justifications like oh, it's just too onerous, and so I think I would like not only the justification, but also a discussion of the kind of weaknesses that might arise because of not using that kind of comparison, as well as any measures taken to compensate for the lack of such a group.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted two, essential for both, and don't have any additional comments.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: I voted two for essential for both of them. They're both consistent with the rigorous methodology and when followed will

improve our ability to decide if it's necessary and reasonable. Thank you.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two and I concur with Dr. Mora.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted two, essential. I am a little concerned about the justification clause with the contemporaneous comparison group, and that, the justification needs to be substantial, such as the service's use is already widely spread in the population so that it's challenging to get the contemporaneous comparison group, but overall two for both criteria.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted one for important. I was a little conflicted like none of the above. I think actually that the 2014 wording is better in many ways. I don't like the focus on CMS decision making in the first bullet, I don't think it's necessary at all.

But the second bullet is better than many of the criteria around sort of good study design, but I think it's important to call out, so that's why I'd sort of eliminate the first bullet and the second bullet would see it through.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted zero, not important, not because conceptually these aren't important aspects, but looking at them together in the totality, I agree very much with what Dr. Whitney just stated, especially around this idea of calling out explicitly decision making by CMS and the lack of, if you've got to justify it, but I think Dr. Kanter said well, okay, it's really hard or extensive to do it. I think there is a lot of work that needs to be done here.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: I voted zero. I might have been tempted to go with a one based on what Dr. Whitney was saying. You know, I agree, bullet one doesn't need to be there at

all, and bullet two is in many ways implied in any reasonable study approach, but I do want to return briefly to this issue of contemporaneous comparison group.

I won't reiterate the full breadth and depth of the argument I tried to make earlier, but this can be used as a slippery slope for RCTs with, you know, placebo control arms for traditionally approved FDA products. That's going to do a lot of harm to Medicare beneficiaries and not necessarily provide a lot of value. If it's just for, you know, a claims data study, people that happen to be on a drug and people that happen to be off, maybe it's a different set of considerations about whether that's okay.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I'm a little torn between one and two to be honest. I think many panelists have said many elements of these are already incorporated, and I think Dr. Whitney said he liked the original criteria and I kind of agree with that. I mean at the end of the day the design has to be methodologically

appropriate. Number of patients, et cetera, presumably that's implicit in some of the other criteria if you want, you know, appropriate outcomes that can generate clinically meaningful data. So I think a lot of this is duplicative.

And the second bullet I just feel, I'm not a methodologist, but I'm a little confused by when that would be appropriate, so I'm a little torn between the two. I like the original criteria better frankly.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: I too would have voted likely not important. I agree with the last four panelists, that almost all of these elements are captured here within other discussed requirements. You now, there was mention of a complete protocol in proposed element E; you know, that would presumably cover some of the aspects, and why we specifically revoked some capacity and bias out of the complete protocol, I'm uncertain here.

Also, elements in the first bullet that speak to safely, I think we discussed with

Dr. Segal and asked what that would cover beyond what is already covered for within 45 CFR Part 46 as well as CFR Part 56, and there wasn't additional language there that would justify an evaluation of safely for Medicare, and certainly it would be mindful of wording like that in the evaluation for Medicare.

If we pushed for the wording, I too prefer the 2014 version of the wording, but would elect to strike and go without, given that these elements are covered otherwise.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted two. In reading the first bullet around generating valid evidence safely and efficiently for decision making, I think this is a nod to innovation and flexibility in study design that it sounds like a lot of members of this committee and also speakers yesterday were looking for, so I like that about this, it makes that explicit. And it doubles down on that by stating if a contemporaneous comparison group is not included, the choice must be

justified. So it's making explicit that there's room for innovation and flexibility here.

And I think likewise for that second bullet, again, this is particularly important when studies are not randomized, so the importance of insuring that there's adjustment for confounding and biases is making that criterion explicit, so I would say two, essential.

DR. ROSS: Dr. Hodes, how did you vote?

DR. HODES: Similarly, I would have voted two for both elements as essential.

DR. ROSS: Okay, thank you for your votes. We're going to move on for number 13. This relates to the theme of subpopulations in the study design. The prior version of the requirement was, the study protocol muse explicitly discuss beneficiary subpopulations affected by the item or service under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria requirements affects enrollment of these

populations, and a plan for the retention and reporting of said population in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.

This has now been, the modified as proposed criteria, in the protocol, the sponsors/investigators describe plans for analyzing demographic subpopulations, defined by gender, age, as well as clinically-relevant subgroups as motivated by the existing evidence. Description of plans for exploratory analyses, as relevant subgroups emerge, is also appropriate to include, but not required. Please cast your votes.

(The panel voted and votes were recorded by staff.)

Waiting on one more vote. Okay, the vote is complete. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential. A few thoughts that I'll share briefly. I think there was something that was lost, I

liked the parts of the 2014 version. I think it's important that we understand how inclusion-exclusion criteria might affect enrollment, that patients in populations that are traditionally underrepresented are enrolled, retained. I think that the current criteria, however, is essential. There are differences oftentimes in the benefits and harms of the various medical services based on gender and age.

I would also suggest that there is an addition, that there is sufficient sample size in order to conduct the various subgroup analyses.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted zero, not important, really kind of influenced by some of our discussion here recently, you know, becoming convinced that the other items that refer to subpopulations and sound methodology basically covers this stuff. And I was a bit put off by the idea that the description of plans for exploratory analyses are explicitly not required. I mean, I was thinking, why

would they not be required. I mean, I would rather they say nothing than say something like that, so I voted zero.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: I voted two, essential. I think it does make good sense in conducting a study in that manner.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I voted two as essential. However, I personally like the wording of the 2014 version, because I think that it's more explicit, and I think that the whole area of health disparities and health inequities is something that needs to be captured as we create protocols or look at study designs. And I think that, I know that it's a difficult area to capture patients in subpopulations and so forth, but I think that there should be some baseline requirements that such data is looked at and included in these different types of protocols that will be developed.

So personally, I think the concept is essential, but I like the wording the way that it is laid out in version 2014 versus the newly

revised version.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential. I think specified plans is really important for accountability, so just a feature of good research practice. I might state a slight preference for the 2014 requirements as well.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted zero, not important, because I think the important piece that is retained in the new version is already in the populations bucket as opposed to the subpopulations, and I prefer referring to it as populations and subpopulations. And the part that I liked about it is gone, which is the idea around paying attention to recruitment of traditionally underrepresented groups in clinical studies, so I think the current version has sort of lost the important part from the old one, and all that's left is already in a different bucket.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: Yeah, I voted one,

important. I felt like the prior criteria really addressed some of the issues that were raised in this one, so I didn't feel as strongly about it in terms of it being essential. Thanks.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two, but I would like to reiterate the comment by Dr. Dhruva as to adequate sample size for the relevant subgroups. I do also believe that the not required should be removed and instead be replaced by required for plans with a large reanalysis of relevant subgroups as they emerge. And then finally, I think the comments in regards to makeup of representative groups should be repeated, but I did vote two.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted two because of the overall importance of some of these concepts, but I do agree that such populations may have been covered by other criteria, and I prefer the 2014 wording.

DR. ROSS: Dr. Whitney, how did you

vote?

DR. WHITNEY: I voted two, essential. I think it's really important that we call this out specifically, even if it may be covered in other areas.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted one, important. I agree with Dr. Fisch, I believe it was Dr. Fisch's comments about we're explicitly calling out something that's not required; if it's not required, we don't need to say it. But I feel like subgroup analyses are actually explicitly required to be laid out on the front end and that's good research design and methodological considerations on the front end of the protocol.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: I voted zero. I would associate myself generally with the comments from Dr. Fresh, or Fisch, excuse me, Ford and Maddox; I know I would trip up trying to say three names. I will also just note -- well, two last quick points. Like many others, I

prefer the 2014 wording. Specifically to the proposed new language, I -- and with apologies if I'm forgetting conversations over the last day and a half. For the life of me, I can't remember or figure out why if we're doing to engage in a listing exercise, why we're only listing gender and age. At least in a prior question we said something like and others as appropriate, or whatever the verbiage was. Here we're listing two and we're not listing race and ethnicity, we're not listing my prior example of IDD and Down syndrome, which are historically marginalized within clinical trials, probably not the only small sub population.

And apologies, one last think. Just referencing the public comments we got about particularly rare and ultra-rare diseases and the complexity of getting the subpopulations there, it's important and valuable to do it. Whether it's feasible from disease to disease may be uncertain at best, and problematic at worst.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I voted two. I think it's important to call this out, even though populations and subpopulations are discussed elsewhere. I do not think the 2014 criteria are appropriate for this day and age, because if you read the wording it really implies wording coming out of a random, out of a clinical trial where you've got that inclusion-exclusion criteria. If we want future studies to be fit for purpose and to be flexible where methodologically appropriate, you may not always have inclusion-exclusion criteria for example, and so I don't like the nature of where the 2014 wording came from, so I would prefer something updated.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: I would have voted zero, not important, consistent with Dr. Maddox's statements.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted two. Originally I did see this as being duplicative of the new criteria J around

representativeness, but as we learned yesterday, this is clearly about taking those representative populations and ensuring that it's clear what subanalyses will be conducted. So I think it's good research practice to do that, and I do think it's not only the demographics that are outlined here but also clinically relevant subgroups.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: I would have voted a two, essential, reflecting the importance of this element and calling it out, despite some overlap with other elements.

DR. ROSS: Okay, thank you for your votes. We're going to move on to item 14, reproducibility. There was no existing requirement and now the proposed criteria is, sponsors/investigators using secondary data will demonstrate robustness of results by conducting alternative analyses and/or using supplementary data. Please vote.

(The panel voted and votes were recorded by staff.)

Waiting on one more vote, and all the

votes are in. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential. I think that there's significant benefit in being able to trust the results when different analyses as well as when feasible different data sources come to the same conclusion.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted one. I agree it's important. I sort of saw it as a nice to have but not necessarily a must have.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: I voted two, essential.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I voted important, and I agree with Dr. Fisch, it's nice to have but not necessarily a required factor.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted one, important. Just a couple comments. I noticed under the reproducibility tag for robustness, we may have discussed this, robustness is a different concept from reproducibilities so you want it

to be, your result to go through even when small parameters change. Second is just the admission of primary data as sort of also having to meet a similar standard.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted zero, not important. I think as Dr. Kanter just said, reproducibility and robustness are different, and so I don't see this as reflective of reproducibility at all, and robustness to me goes under the methodological question around how you deal with confounding and bias, and sort of the, you know, the methodologic rigor of your approach, so I don't know that this adds a bunch, and I think it's mistitled.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: Well, that's a tough one to follow after Dr. Maddox. I voted two, only because it felt like it was a bit more focused on what we're trying to achieve, which is we want the use of any secondary data to be reliable and to be rigorous enough to allow us to draw conclusions about the intents, so thanks.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two, and I agree with the comments made by Drs. Kanter and Maddox.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted one for important. Although I think this type of investigation can be very important, they may not be essential under the application. And if we're concerned about the time that the CED process takes, then I think this requirement should only apply in cases where there would be concerns about either reproducibility or robustness, although those are separate concepts.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted two. I thought it was an important separate callout for the reasons mentioned before.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted one, important.

It is important to understand how to deal with secondary data, but I agree with, I think it was Dr. Kanter's statement about robustness versus reproducibility, and these two concepts are getting merged kind of inappropriately here, I think.

DR. ROSS: Dr. Kremer, how did you, or sorry, Mr. Kremer, how did you vote?

MR. KREMER: That's okay. So, I'm again predictably a zero on this, and I would just generally associate myself with comments of the various actual doctors that said one and zero, but with similar emphasis on Dr. Stearns' point as well.

DR. ROSS: Thanks, and you can see I do need another cup of coffee. Mr. Patel, how would you have voted?

MR. PATEL: I would vote with Dr. Stearns, I don't know if she voted one or two, but I would vote one but completely agree, this is obviously appropriate.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: Yeah, so I would have voted a one. I agree fully with Dr. Kanter and

Dr. Maddox on all points raised.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted a one, I think it's important but not essential. I would also recommend a wording change. I would probably use the term sensitivity analyses instead of the term alternative analyses.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: I would have voted one, in association with the comments made by Dr. Kanter.

DR. ROSS: Okay, thank you for your votes. We're going to turn to item 15. In the interest of time, I'm not going to read the prior criteria, which is lengthy. I'm going to just reinforce the proposed criteria which is, the study is submitted for peer review with the goal of publication using a reporting guideline appropriate for the study design and structured to enable replication. Please cast your votes.

(The panel voted and votes were recorded by staff.

Okay, all the votes are in.

Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential. A couple of notes I made. First, this element, this item doesn't mention results reporting, which is mandated legally by clinicaltrials.gov compliance, but I think that it's important that the study be submitted for peer review with the goal of publication, but the results, the study and its results can be made available through a variety of other methods such as preprints. We've seen unfortunately a lot of publication bias because of negative results, and I think it's an ethical duty to study participants that the results be made publicly available.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted number two, that it's essential. You know, I was thinking about -- well, Dr. Segal made the point yesterday that there was some consideration about requiring publication but that CMS can't really control the publication process and timetable, and she explained that peer review

is kind of like a surrogate for a product that could be discernible and that may or may not always be the case, but I decided that this was as good as we could do and voted two.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: I voted two, essential. I agree with the above.

DR. ROSS: Dr. Ford, how did you vote.

DR. FORD: I voted two, and I also agree with the previous comments.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential. I will say I am, I don't think the criterion of submission is sufficient. I mean, I can click the mission to nature as well as the next person, but I don't think that's a good proxy for peer review, so I might actually strengthen it to have some form of publication if peer review is the objective. There are open access and other journals that do focus on the regular methodology rather than the so-called significance of the outcomes, so I think there are venues available for that.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted two, essential, but I would agree that it's necessary but not sufficient. The goal should be making sure that the results regardless of the findings are made accessible broadly, and undergo some sort of review. So I don't think this goes far enough, but I think it's an essential concept. I also appreciate the language talking about the appropriate for the study design to that it clears, you know, if we have observational data, again, to get away from the clinical trial approach, and I appreciate that wording, appropriate for study design, but I think it doesn't far enough in requiring the results be made available.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: I voted two, essential, and agree with prior comments.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two, and I agree that just submitting for peer review is not enough, there needs to be some

strengthening of this requirement to push them to peer review avenues that will test for reproducibility and hopefully the data can be made public.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted two for essential, and I have the same concerns expressed by others in that the being submitted for peer review seems like not being enough.

I'm going to provide two comments to CMS, and one of those has to do with the possibility of consideration of mechanisms such as Registered Report. I sent a link around, on that yesterday. And then I'm also going to send CMS a link about this issue of negative publication bias.

But I'm okay with the current wording because I think it's a compromise and that requiring publication is not possible.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted two, essential. I think the notion that it's going to end up in the published literature is really important.

I would point out that the way it's worded, is it possible to satisfy at the outset of a CED, because it says it's already submitted and it hasn't even started yet, so you may want to look at how the timing works in terms of the wording.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted two, essential, and echo the comments that likely this does not go far enough.

DR. ROSS: Mr. Kremer, how did you vote?

MR. KREMER: I voted zero predominantly for the reasons that I explained in our open discussion before the voting, but I will just reiterate one point. While I think we have consensus that peer review and transparency are critically important to the field, my concern here is about how this is implemented and if this winds up extending the time after which it is clear from the evidence that there is a reasonable and necessary degree of benefit for patients, that this extends the period of time before they can actually get it.

And it's those periods of delta that really scare me. Before a study is even started and no one has access, even those who would be enrolled in it, in a CED trial and after that trial has been completed but before a reconsideration process is engaged or completed by CMS, you've got a big window of time where patients lose out on benefit to which they ought to be entitled in a timely fashion.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I would have voted two. I agree with Dr. Whitney, the phrasing should be the study will be submitted, if the study has been completed, but I also think about this requirement in conjunction with criterion Q, in which we were expecting the data to be delivered to CMS.

And I think to the point that Mr. Kremer just made, you know, in terms of the delay, presumably, and maybe we're talking about it in terms of criteria Q, but if CMS has the data in a timely manner, they can negotiate a reconsideration while the publication process

goes on. So I kind of think a little bit about the two together, so transparency is clearly necessary if there's a (break in audio) negative understand sort of a publication bias taking place here. But hopefully, the fact that CMS will had the data under criterion Q will offset some of that and give us the transparency that I think would satisfy that component.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: I would have voted two. Actually, Dr. Kanter's and Dr. Maddox's, their sentiments there, as well as the considerations around the timing as Dr. Whitney mentioned, the time that CMS had to make a decision on improving CED studies, it's more of a commitment that the individuals making the sponsor/investigators to submitting these, as opposed to them actually occurring.

You know, just a bit of a caution too on timely information to Medicare. I think it's important that this is all in a public space whereby, you know, reconsideration or otherwise, Medicare makes, I don't believe can

be made off with data that they're reporting uniquely that has to be part of the public realm, so certainly wouldn't down prioritize this reporting on item 15 in any way.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted two, and I echo the comments of Dr. Canos.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: I would have voted two, essential, and I agree with those who suggest that submission for peer review is necessary but not sufficient and the reexamination, there are other ways to make data publicly available even before a formal publication. We have concerns that were just expressed about having data made available to CMS, I doubt that CMS would want to be in a position of having private data to which only it had access to, on the basis of rendering a decision.

DR. ROSS: Thank you for your votes. We're going to move on to criterion 16, under the theme of sharing for which there was no existing requirement previously. The proposed

criteria is, the sponsors/investigators commit to sharing analytical output, methods and analytical code with CMS or with a trusted third party in accordance with the rules of additional funders, institutional review boards and data vendors as applicable. The schedule for sharing is included among the study milestones. The study should comply with all applicable laws regarding subject privacy, including Section 165.514 of the Health Insurance Portability and Accountability Act of 1996, otherwise known HIPAA. Please cast your votes.

(The panel voted and votes were recorded by staff.)

We have one more vote. There we go. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential I think this is an essential requirement with the addition that Dr. Kanter pointed out in her questions earlier today that this does not include data sharing, which is obviously absolutely essential in order to be able to use the methods and the analytic code to be able to arrive at an outcome.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted two, essential also. I think the public would appreciate if the kind of spirit of trust were verified.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: Two, essential. Transparency is very important.

DR. ROSS: Dr. Ford, how did you vote?

DR. FORD: I voted essential as well, and I agree that transparency with the public is very important.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted two, essential, and I did want to strengthen it to include data as well as the output methods in the code.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted one, important, because as written without reference to data, I don't think it does much, code is sort of useless without knowing what it does, but I completely agree that this concept is crucial.

DR. ROSS: Dr. Mora, how did you vote?
DR. MORA: I voted two, essential, it promotes transparency and trust.
DR. ROSS: Dr. Stearns, how did you vote?
DR. STEARNS: I voted two, essential, and I agree with a comment that was submitted by the researchers at the Schaffer Center, which is that taxpayer-funded data collection mandates should require to the extent possible that the identified data should be made publicly available as soon as ethically or reasonably possible.
DR. ROSS: Dr. Whitney, how did you vote?
DR. WHITNEY: Two, essential. I agree with the prior comments.
DR. ROSS: Dr. Riddle, how did you vote?
DR. RIDDLE: Two, essential, and I would implore CMS to require data sharing as well, as has been mentioned by others.
DR. ROSS: Mr. Kremer, how did you vote?
MR. KREMER: I voted zero.

Transparency, incredibly important, I agree with all my colleagues on that. I would just reiterate my previous point that transparency like so many other things, needs to be a two-way street, and while sponsors/investigators owe all of us transparency, CMS owes us greater transparency than we have gotten historically, and more transparency than I fear we will get looking forward about how they reach decisions, either to initiate CED, or whether to reconsider or whether a reconsideration results in coverage or non-coverage. So the entire system holistically and contemporaneously needs to be much more transparent.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I would vote two. I would urge a little bit of caution on the data piece, data sharing piece as I mentioned earlier today or yesterday, around some of the sources of data that may actually not allow that to happen. I do think it's important to share the analytic outputs and code, I've said that.

And I think the other change I would

make goes back to the protocol submission. So when we talk about sharing, included among the study milestones, maybe put in a requirement that basically says, you know, if the protocol is submitted and not published within the appropriate time, then CMS does have the ability to make public the analytic output, and basically then initiate an NCD. So I think there can be something crafted where you push for the protocol submission and hopefully publication, but if not, CMS retains the right to fully make the analytic output public in some way, so that the NCD process can continue frankly.

DR. ROSS: Thank you. My apologies, Dr. Ogunwobi, I thought I called on you, but Tara sent me a message saying I did not ask you your vote and rationale.

DR. OGUNWOBI: Yes, I voted two, and I agree with the comments that it does not go far enough, transparency is critical.

MR. ROSS: Okay. I apologize for following along with a pen. My apologies.

Dr. Canos, how would you have voted?

DR. CANOS: I would have voted two

with the wording as stated up until the last sentence on the session applies, and I'm a little unclear if sharing this information with CMS is actually a study activity or something done after the study itself, so compliance of the study with applicable laws, I'm wondering if it actually falls, you know, under J and other things stated within the requirements.

Additionally, you know, as stated during the discussion period, uncertain if HIPAA would really be applicable for a sponsor in this case as far as the data sharing goes, and ultimately it's the sponsor/investigator that the CED study is being approved for and the requirements are upon, so I, if we did state something about the applicable laws, that I would mention sharing of data in compliance with applicable laws and allow for, you know, CMS or others to, you know, CMS can make sure that these are in line with the laws for the sponsor/investigator.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: I would have voted two, and I have no new comments to add.

DR. ROSS: Okay. Dr. Hodes, how would you have voted?

DR. HODES: I would have voted two with a suggestion for additional inclusion of data.

DR. ROSS: Okay, thank you for your votes. Moving on to the last item which I expect will actually be, but maybe I'll be surprised, the least controversial, this is the theme of legal.

The prior criteria was, the study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Such studies may meet this requirement only if the disease or condition being studied is life threatening as defined in 21 CFR 312.81(a) and the patient has no other viable treatment options.

The proposed criterion now up for the vote is, the study is not designed to exclusively test toxicity, although it is acceptable for a study to test a reduction in toxicity of a product relative to standard of care or an appropriate comparator. For studies that involve researching the safety and

effectiveness of new drugs and biological products aimed at treating life-threatening or severely-debilitating diseases, refer to additional requirements set forth in 21 CFR 312.81(a). Please cast your votes.

(The panel voted and votes were recorded by staff.)

Waiting for one more vote. Okay, the votes are all in. Dr. Dhruva, how did you vote?

DR. DHRUVA: I voted two, essential. I think this is a reasonable and essential requirement.

DR. ROSS: Dr. Fisch, how did you vote?

DR. FISCH: I voted one, that it's important. It does seem kind of redundant to the extent that we're talking about net benefit, net person-centered benefit. I think it sort of implies that pathophysiology or toxicity only might not meet that criteria, but I voted one.

DR. ROSS: Dr. Flannery, how did you vote?

DR. FLANNERY: I voted one, it's

important but not essential. It's not fully understandable, why the first sentence is necessary.

DR. ROSS: Dr. Ford, how did you vote.

DR. FORD: I voted that it was important, and I also agree about, that it's also implied in other sections of the report regarding the actual benefit to patients, so my vote was important, number one.

DR. ROSS: Dr. Kanter, how did you vote?

DR. KANTER: I voted one, important. I also am not sure I understand the full implication, but if the issue is just simply testing toxicity or safety, one can imagine, you know, there are scenarios where you're translating FDA studies to the Medicare population where safety is the central issue, as opposed to efficacy.

DR. ROSS: Dr. Maddox, how did you vote?

DR. MADDOX: I voted one, important. I'm not sure I totally understand, since the first sentence seems to say it shouldn't exclusively test toxicity unless it's testing

related to something else? Maybe I just don't understand it, but it didn't feel like something that needed to be essential.

DR. ROSS: Dr. Mora, how did you vote?

DR. MORA: I voted one, important, and I don't have any additional comments to add. Thanks.

DR. ROSS: Dr. Ogunwobi, how did you vote?

DR. OGUNWOBI: I voted two, and I agree with Dr. Dhruva.

DR. ROSS: Dr. Stearns, how did you vote?

DR. STEARNS: I voted one, largely for reasons given. I kind of understand it's important, but I would think toxicity would have been covered by other criteria.

DR. ROSS: Dr. Whitney, how did you vote?

DR. WHITNEY: I voted zero, not important. I think it's addressed in all the prior criteria around proper outcome selection, net clinical benefit, yadda, yadda, yadda. Then there's a big, you know, obvious exception clause here that would be the principal space I

would expect this to be considered. So it's essentially saying don't do it unless you mean to do it, and then it would meet the prior criteria, so not important.

DR. ROSS: Dr. Riddle, how did you vote?

DR. RIDDLE: I voted two, essential, but I'm not sure I agree with myself actually after listening to the comments for this. This is confusing to be completely honest, and I think maybe could completely get struck altogether, to be completely honest with you guys.

DR. ROSS: Okay. Mr. Kremer, how did you vote?

MR. KREMER: Well, with a shout out to Dr. Riddle for his flexibility where I'm showing none, I'm voting zero again. But with that said, generally I agree with Dr. Whitney on the rationale. If I weren't going to vote zero for other reasons, I'd vote zero for Dr. Whitney's reasons. That said, I sort of appreciate, notwithstanding the uncertainty about that second clause in the first sentence, I kind of appreciate the shout out to having

some reason to test reduction of toxicity, because I don't think that's as evident in the existing language, so I'm still a zero.

DR. ROSS: Mr. Patel, how would you have voted?

MR. PATEL: I guess a one. I meant, if the requirements in 21 CFR have to be there, they have to meet all other applicable laws, I thought we said somewhere else. I'm not sure why they need an additional call out.

DR. ROSS: Dr. Canos, how would you have voted?

DR. CANOS: One, and agree with Dr. Maddox as far as the lack of clarity around the first sentence.

DR. ROSS: Dr. Umscheid, how would you have voted?

DR. UMSCHEID: One, and I echo the comments of Dr. Patel.

DR. ROSS: Dr. Hodes, how would you have voted?

DR. HODES: Similarly, one, same comment.

DR. ROSS: Okay, thanks for your votes.

That actually brings us to the end of the voting questions portion of our meeting.

Does anyone have anything they would like to add as a conclusion before we bring this meeting to a close and I turn it back over to CMS? Mr. Patel?

MR. PATEL: Dr. Ross, I want to commend you for doing a great job. You got us through two days on time, with not a lot of confusion and everything else, so kudos to you, and hopefully you get another assignment in the near future to do this again.

DR. ROSS: Thank you. I only skipped a couple people going around; I realized I'm not very good at factory work, but doing the same thing over and over, my mind wandered.

Dr. Ford, did you have a question or want to make a comment?

DR. FORD: I actually had a question. I was just curious. How will all of the comments and suggestions be dealt with?

DR. ROSS: That's great, thank you. And of course I want to thank the entire committee for being so thoughtful and insightful and attentive throughout the two

days, offering numerous comments and suggestions to CMS.

The steps, the path forward is, all of the information, everything we've said, all of the votes we've taken, everything has been recorded and is being transcribed for the CAG team to take into consideration as they take the AHRQ report into consideration along with the proposed criteria. These are suggestions to CMS to modify their coverage with evidence development criteria.

The report was asked for or requested by CAG. Now with the sort of recommendations in hand from AHRQ and our comments and suggestions in hand, they will then ideally put together a final, or a near draft sort of proposal, and the CAG team can chime in on this, but they put that together and that will then go out for public comment before any CED criteria are finalized.

But that's the step forward. So everything that's been said throughout the meeting, both by members of the committee and members of the public, is now in the record for CMS to consider.

Dr. Mora?

DR. MORA: Just a quick shout out as well to all the team that helped coordinate and get us all prepared for this. I know that I needed a little extra support and reminders, and they did a great job. And once again to you, Dr. Ross, thank you for your facilitating leadership, engaging us all, and working us through this complex process. Appreciate it.

DR. ROSS: Thank you again.

Mr. Kremer?

MR. KREMER: So I'll just reiterate the thanks to you, Joe, for your leadership, and I of course want to thank all my colleagues voting and nonvoting on the panel, but I particularly want to thank CMS and the CAG for having me here.

Clearly I am a dissenting voice, not of the substance but on the fundamentals, the question about whether CMS even has authority, and CMS did not have to allow me to be part of this panel, but I appreciate listening not only to my point of view whether it changed any votes or not, whether it changes the outcome or not, I appreciate the opportunity to try to

influence the process. And more important than that, I appreciate the CAG, CMS and all of the panel members, again voting and nonvoting, doing their level best to take to heart the public comment, which is far more important than anything I might have said during the last two days. If this is about anybody, it's got to be about Medicare beneficiaries themselves, and secondarily about their family members and any other ecosystem of support, and if this process serves them, then we'll figure out how to surmount whatever the regulatory and statutory issues might be about authority, but if it doesn't serve them, then we've got to find a process that does.

DR. ROSS: Tamara or Tara, do you have any concluding comments for the committee before we adjourn? Did we get through everything you needed us to?

MS. JENSEN: Oh, thank you, everyone. Very impressive, we were able to get through 17 questions in one day, so that is a record for a MEDCAC panel.

And so next steps, I think we're getting questions from the public as well as

all of you. So the next steps are what Dr. Ross just outlined, which is we're going to take all of the comments and how the transcript is very important, that will be made public sometime probably early next -- not the transcript because it needs to be transcribed, but everything you've said today, the votes and everything will be public next week.

If CMS working with our partners at AHRQ decides to update the coverage with evidence development criteria, the next step would be that we would issue a guidance document as allowed under the statutes, under the process we have outlined in our Federal Register notice. So we would issue the guidance document, there would be a public comment period, and then we would issue a final guidance document in answering the public comment.

So again, a lot of opportunities, this will be the third opportunity for the public can to weigh in on the CED criteria.

This meeting is essential for us to decide, you know, how we're going to, what we might update if we update all of those items on

there. So again, really, thank you, everyone, for weighing in and helping us move to update and improve the criteria, as well as all the comments in the process, which we also take a look at. I hope everyone has a wonderful week after the last two days.

MR. KREMER: Tamara, I apologize. I put a quick question in chat, I apologize for it being after your closing, but will there actually be a video recording posted for the public at some point for those who would benefit from more than a raw transcription?

MS. JENSEN: I don't know.

MS. HALL: Yes, there will be.

MR. KREMER: Great, thank you, and again, apologies for the last-minute question.

MS. JENSEN: That was a good question, thank you.

DR. ROSS: Thanks again to all my colleagues for making the time to spend ten hours for the past two days discussing all of these criteria and all the time in advance.

Enjoy the rest of your day and take care. Thank you.

(Whereupon, the meeting adjourned at

2:57 p.m. EST.)