Draft Guidance: Incorporating Voluntary Patient Preference Information over the Total Product Life Cycle
October 15, 2024

Moderator: CDR Kim Piermatteo

CDR Kim Piermatteo: Hello everyone, and welcome to today's CDRH webinar. Thanks for joining us. This is Commander Kim Piermatteo of the United States Public Health Service, and I serve as the Education Program Administrator in the Division of Industry and Consumer Education within CDRH. I'll be the moderator for today's webinar.

Our topic today is the draft guidance titled, Incorporating Voluntary Patient Preference Information over the Total Product Life Cycle, which was issued on September 6th, 2024. FDA is issuing this draft guidance to communicate when and what methods could be used to collect and submit patient preference information, or PPI, across the total product life cycle.

I'd now like to introduce our presenter for today's webinar; David Gebben, Health Economist within the Division of Patient Centered Development within CDRH's Office of Strategic Partnerships and Technology Innovation.

We'll begin with a presentation from Dave and then field your questions about this draft guidance.

Before I turn it over to Dave, I'd like to provide a few reminders. First, please make sure you've joined us through the Zoom app and not through a web browser to avoid technical issues. Second, the intended audience for this webinar is industry. Trade press reporters are encouraged to consult with the CDRH trade press team at cdrhtradepress@fda.hhs.gov. And members of national media may consult with FDA's Office of Media Affairs at fdaoma@fda.hhs.gov.

Third, for those of you who might want to follow along, you may access printable slides of today's presentation from CDRH Learn at www.fda.gov/training/cdrhlearn under the section titled How to Study and Market Your Device, and the subsection Cross-Cutting Premarket Policy. And lastly, we look forward to interacting with you during the live question-and-answer segment of today's webinar. If you have a question, please wait and raise your hand at the end of today's presentation to get into the queue.

Thank you all again for joining us. I'll now turn it over to Dave to start today's presentation.

David Gebben: Thank you again for joining today's webinar on the draft guidance titled, Incorporating Voluntary Patient Preference Information over the Total Product Life Cycle. This draft guidance is part of our commitment in Section 5E of the Medical Device User Fee Amendments, Performance Goals, and Procedures for Fiscal Years 2023 through 2027, MDUFA V.

This guidance, when finalized, is intended to provide updated recommendations to industry and FDA staff for designing, collecting, and evaluating patient preference information referred to as PPI during this presentation. In the context of benefit risk assessments of medical devices, this includes practical recommendations intended to address common questions for those interested in the voluntary inclusion of PPI for FDA consideration.

The learning objectives for today's webinar, as related to the draft guidance on Incorporating Voluntary Patient Preference Information Over the Total Product Life Cycle, are to explain the rationale for why CDRH has incorporated these updates to the 2016 PPI Guidance that is currently issued, to lay out the scope of these updates, describe the modifications, and finally, to describe how to submit comments on the draft guidance.

CDRH has a history of commitment to advancing PPI methodology and its potential use in the regulatory context, as demonstrated by our guidance, language, research, and partnerships. I'll highlight the most relevant points as related to the updates in the draft guidance. In March 2012, the original benefit-risk guidance was issued. The 2012 Benefit-Risk Guidance was the first to mention that risk tolerance varies for patients, and preferences can shed light on how that variation can be included in the benefit-risk determination.

In 2013, interested parties representing academia, regulators, patients, and the medical device industry gathered to discuss how PPI could be incorporated into the regulatory process, serving as complementary evidence along with data from clinical and non-clinical studies that may be submitted at both pre and postmarket time points. The discussions at the workshop centered on the state of the science of patient preferences and advanced discussions on the methodology and validation considerations needed to use PPI in a regulatory context. This marked the beginning of a greater focus on the value of PPI in regulatory submissions and highlighted the need to advance the methods.

In January 2015, the obesity device preference study was published. This PPI study was considered in the benefit-risk assessment of the first medical device approved to treat obesity in almost a decade. This instance opened the door for future submissions that included PPI as a complement to other forms of scientific evidence by providing a case example for interested parties of how PPI can be used in a regulatory context.

In 2016, CDRH issued the final PPI guidance. This guidance provided recommendations for conducting high quality patient preference studies as well as detailed potential uses for this voluntary information in medical device evaluations.

Since the 2012 Benefit-Risk Guidance and the 2016 PPI Guidance, FDA has issued other guidance documents that mention the usefulness of PPI during benefit-risk determinations for investigational device exemptions, premarket notifications, 510(k), and postmarket decisions such as compliance and enforcement decisions and when assessing the impact of uncertainty during benefit-risk determinations.

CDRH Partnered with ISPOR in September 2020 to jointly host a summit discussing the use of PPE in medical device regulatory benefit risk determinations and beyond the regulatory context. The summit provided an instructive foundation for PPI where multidisciplinary participants engaged in robust discussions on current methodological issues, the implementation and application of PPI, and the potential uses of PPI beyond the regulatory arena.

Several PPI case studies shared by medical device companies highlighted diverse uses of patient preference studies created to inform the design of clinical trials and impact the benefit-risk the decision. All of these moments have built towards helping build the foundation of why we have revised the draft guidance. Going forward, CDRH recognizes that PPI is an evolving field. CDRH will continue to maintain

its commitment to the potential use of PPI in the regulatory context, as demonstrated by our guidance, language, research, and partnerships.

The original 2016 CDRH PPI Guidance focused on the benefit-risk decision point to support marketing regulatory decisions. Since that time, new guidances have been issued, and these guidances have expanded to reflect the total product life cycle. This update also reflects additional considerations and practical recommendations on evaluating PPI that resulted from the interactions with sponsors and additional CDRH funded PPI studies. This draft also addresses a MDUFA V commitment.

Some principles have been maintained from the 2016 version. The definition of patient preference information remains unchanged. It is still defined as qualitative or quantitative assessments of the relative desirability or acceptability to patients of specified alternatives or choices among outcomes or other attributes that differ among health interventions.

Further, the revised guidance maintains a focus on PPI research as patient centered. As such, best practices in survey research would still apply, like patient friendly descriptions of options and clear, balanced presentations of choice tasks. The expectation that research will be done in line with recommended practices from professional organizations is also maintained.

We will now turn to the rationale for the updates.

In 2023, CDRH issued a Federal Register Notice requesting feedback on questions posted about the potential guidance update. From these comments, we were able to incorporate some of the observations into the current draft. It was also noted that there were several remarks asking about greater clarity on analysis methods.

The gaps identified through interactions with sponsors include things like the role that qualitative methods could play, the types of quantitative methods available, and what is considered a fit-for-purpose PPI study. A common question in submissions was about the attributes and attribute levels that should be included. Other questions were related to defining research questions that would be in alignment with FDA regulatory needs.

It was also noted that there was a request to have greater clarity on what would be helpful to include in a PPI study protocol that is submitted for FDA review. Finally, there was an opportunity to clarify the value of having early interactions with the FDA.

The draft guidance broadens the scope of where PPI could be applicable. As previously mentioned, the 2016 Guidance primarily looked at the benefit-risk decision after clinical performance data had been collected and at the point of marketing submission or decision point. The current draft guidance encompasses the total product life cycle. Patient preferences may have a role at multiple spots along the total product life cycle. This includes such points as discovery and ideation through innovation and prototyping, pre-clinical regulatory decisions, and potentially postmarket monitoring. This input can be provided along the entire TPLC rather than just a benefit-risk determination.

These are potential opportunities to use PPI at different phases of the product life cycle. For instance, during development, PPI methods such as focus groups could be used to identify an unmet medical need. During the clinical design phase, if a product has multiple potential endpoints, the patient voice

can be incorporated as using a best to worst scaling method to inform which endpoints are of greatest importance to the patients. During the postmarket phase, patient preferences could provide information on how potential unknown risks are viewed by the patient population.

What are the updates that have been incorporated into the new draft guidance? On the following slides, we will discuss what some of those key changes have been.

Perhaps right at the top, it ought to be noted that the new draft guidance has a new name to reflect the opportunities CDRH sees to incorporate the patient voice through PPI across the total product lifecycle. We also responded to the feedback for a larger number of practical examples, so we added more examples to this draft guidance update.

In response to requests to discuss methods in greater detail, we added an appendix listing possible methods that could be applicable. We received questions regarding fit-for-purpose while we maintained the principle of patient centricity in PPI studies from the 2016 Guidance. We highlight the importance of the scientific question, discuss the study objectives, and the study parameters, all of which contribute to the determination of if a study is fit-for-purpose. Finally, we expanded the draft guidance to other places along the TPLC, including IDEs or 510(k)s.

In 2016, there was a more limited number of use cases for PPI. In 2016 Guidance, the primary use case was the obesity study, which focused on the benefit-risk decision context after clinical data had been provided. Since that time, several additional studies have been done, including a label expansion, understanding how or what a clinical effectiveness threshold would need to be for a new treatment option. This expanded list of examples, while not meant to be exhaustive of the potential for PPI within a regulatory context, it is meant to show that patient preferences can be used in many locations throughout the total product life cycle. Further, we have maintained the hypothetical examples in the draft guidance.

Throughout the process of reviewing PPI submissions since 2016, a number of sponsors, as well as docket comments, sought greater clarity on what analysis methods would be appropriate for quantitative preference data. To respond to those comments, we incorporated an appendix to list potential analysis methods. This appendix is not meant to be an exhaustive list, nor is the appendix meant to be a cookbook for how to do the analysis. CDRH recognizes that analysis methods change and improve through time, and the appendix is not meant to be a final word on analysis methods. Rather, it is intended to provide a starting point for potential analysis of quantitative preference data.

Multiple sponsors and docket comments requested clarity on what goes into the consideration to determine if a study rises to the level that could be considered fit-for-purpose. To that end, an additional section 4I titled, What Important Factors Should Sponsors Consider When Designing a Patient Preference Study to Address an FDA Decision Making Question, was added. This includes discussion of considerations related to the scientific question and study objectives and parameters.

Along with that, other considerations are how and where qualitative or quantitative methods could be incorporated, how the indication for use population is reflected within the study population through aspects such as the enrollment criteria and various recruiting methods. If a survey method is used, information on the specific survey design is relevant to be included in the submission packet.

Here are other guidance resources I mentioned earlier in the presentation, along with the full URL that you can access after the presentation.

You may comment on any guidance at any time per 21 CFR 10.115(g)(5). Please submit your comments before December 5, 2024. This will ensure that the FDA considers your comment on the draft guidance. We welcome your comments and feedback on the draft. We recognize that the PPI field is continually improving and your suggestions to help refine the PPI guidance are greatly appreciated.

In summary, the updates reflected within the draft update the guidance to reflect the state of PPI today and recognizes and reflects the concerns from sponsors and other interested parties. This revised draft guidance aligns with more recent published guidances to fit within the overall guidance ecosystem. The modifications are intended to add clarity and fill gaps that were observed in the 2016 PPI Guidance. Finally, the scope has widened for PPI to the entire TPLC to encourage the patient voice to be heard more clearly and more often throughout the entire TPLC. Thank you for your time. I look forward to your questions during this webinar and reading your comments and feedback posted before December 5, 2024.

CDR Kim Piermatteo: Thanks for that presentation, Dave. At this time, we will now transition to our interactive question-and-answer segment.

So joining Dave today, we have a few additional panelists to assist with your questions. First is Olufemi Babalola, Health Economist in the Division of Patient Centered Development within the Office of Equity and Innovative Development in CDRH's Office of Strategic Partnerships and Technology Innovation, or OST; Cynthia Grossman, Division Director for the Division of Patient Centered Development within the Office of Equity and Innovative Development in OST; and Kathryn Capanna, Associate Director for Strategic Initiatives in OST as well. Thank you all for joining us.

Before we take our first live question, I would like to go over how we will manage this segment and a few reminders. So first, to ask a question, please select the Raise Hand icon, which should appear on the bottom of your Zoom screen. I'll announce your name and give you permission to talk. When prompted in Zoom, please select the blue button to unmute your line and then ask your question.

When asking your question, please remember to limit yourself to asking one question only and try to keep it as short as possible. And we appreciate that you may have a very specific question involving your device or company or scenario; however, we might not be able to answer such specific questions during today's webinar. Therefore, we will try to frame a broader response based on what's described in this draft guidance. After you ask your question, please lower your hand in Zoom. And if you have another question, please raise your hand again in Zoom to get back into the queue and I will call on you as time permits.

Before we take our first live question, I would like to ask our additional panelists some additional questions that we've previously received about this draft guidance. And so the first question I would like to direct towards Femi. Femi, the question that I have for you is, what role do you see PPI playing in the development of clinical trials for medical devices?

Olufemi Babalola: Thank you, Kim. I see the role of PPI in clinical trials as potentially helpful to illuminate what endpoints or what levels of effectiveness or risk would be deemed acceptable. It would

depend on where in the process the sponsor is. The exact area of application would also be dependent on the product and the research question. Thank you, Kim.

CDR Kim Piermatteo: Thanks, Femi. Cyndi, next I'm going to come to you with a question. Cyndi, that question is, could you comment on how PPI can or could be used in the postmarket phase?

Cynthia Grossman: Yes. Thanks so much, Kim. So one example of the use of PPI in the postmarket phase is for expansion of an indication. So one of the examples that we had was for at-home hemodialysis device, where the company relied on a threshold technique, one of the specific stated preference PPI methodologies, to expand their device indication for home hemodialysis to be solo. So that's without the use of a care partner. So importantly, this case study demonstrated that a subset of patients-- not all patients, but a subset of patients, preferred solo home hemodialysis, and it also provided evidence of the risk thresholds that patients were willing to tolerate in the case of solo home hemodialysis as a therapy option. So thanks, Kim.

CDR Kim Piermatteo: Thank you, Cyndi. Katie, the next question I have is for you. And Katie, that question is, how do least burdensome principles apply to PPI studies?

Kathryn Capanna: Thanks, Kim. I'll answer generally and then I'd also like to ask Dave to provide a PPI specific example to this. So CDRH does apply our least burdensome principles to all of our activities pertaining to regulation of medical devices, both pre and postmarket. And this is articulated in our 2019 guidance on the least burdensome provisions which outlines three guiding principles. So the first is that we will request the minimum information necessary to support a decision. The second is that we would accept the most efficient means of obtaining that information. And the third is that we focus on getting the right information at the right time. And so for patient preference information, this continues to be voluntary and completely up to the discretion of the sponsor.

But what we have seen is that there are scenarios across the total product life cycle where industry is interested in conducting these voluntary patient preference studies to support their overall evidence package to the FDA. And CDRH is always open to discussion about different ways to more efficiently collect the minimum information that's necessary to support any given decision point. And so when sponsors are designing a preference study and maybe receiving CDRH feedback on the approach to that, they can always propose alternatives. As far as timing, this guidance adds clarity in terms of where in the total product life cycle, a preference study could be useful to industry and to FDA's decisions. Dave, do you have anything to add?

David Gebben: Yeah, I would just add to that-- thank you, Katie-- that when we consider the decisions, for instance, regarding recruitment or other factors that might need to be considered, with recruitment methods, we would expect it to be in alignment with what would be needed. So something that would align with the intended use population. Now, if that was thought that a self-report would be all that it is needed, then that would be sufficient. However, if the disease condition was more specific, then in order to ensure that the correct population is recruited, in that situation, a physician confirmation recruitment method might be expected. But of course, these would have to be determined more on almost a case-by-case basis. Kim, over to you.

CDR Kim Piermatteo: Thanks, Katie, and thanks, Dave. I appreciate everyone's responses to those previous questions we received. So first up, our first live question is coming from Bennett. Bennett, I have unmuted your line. Please unmute yourself and ask your question.

Bennett Levitan: Thank you. The draft guidance refers to including preference information and decision summaries and device labeling, but I don't recall if there's ever been an example of a label doing that other than the Genentech example. Do you have examples of that or are you going to add an example of label with preference information to the guidance?

David Gebben: I'll take a first pass at answering that great question from Bennett. To this point, we do not have an example of labeling. We have included that because we recognize that it is a potential, but at this point, we do not have anything included as a specific, and at this point, I don't envision anything being added.

CDR Kim Piermatteo: Thanks, Bennett, for that question, and thank you, Dave, for that response. Okay, so I encourage everyone, if you have a question, please feel free to raise your hand in Zoom and I will call on you and you can interact with our panelists today. I'm going to come to Cyndi next with a previous question we received as well. And Cyndi, that question is, within the broader patient science context, how will this draft guidance relate to potential clinical outcome assessments developments?

Cynthia Grossman: Thanks, Kim. So as some of the my co-panelists have suggested and indicated, things are on a case-by-case basis in terms of the specifics. But in general, the Division of Patient Centered Development is focused on advancing patient science methods. That includes patient preference information, clinical outcome assessments, and patient reported outcomes in particular, and also collaborating with other centers, for example, on the patient focused drug development guidances.

But the PPI guidance specifically reflects the potential use of this methodology across the total product life cycle and is seen as part of that whole complimentary package of different ways to assess the patient-- to advance patient science methodologies and patient centered development, including patient clinical outcome assessment development as well. So it's part of that whole package of the different types of patient science methodologies, and there's specific use cases obviously pointed out in the guidance and examples. In the PPI guidance.

CDR Kim Piermatteo: Great. Thanks for that. Sorry. Thanks for that, Cyndi. Alright, I'm going to go ahead and go back to Femi with another question that we have previously received. And Femi, that question is the draft guidance talks about fit-for-purpose studies. Can you describe a research question that might lead you to a specific PPI method mentioned in Appendix B?

Olufemi Babalola: Thank you very much, Kim. As Dave said of note in his presentation, there are key aspects of a fit-for-purpose study that we look at and that was listed in the guidance. One aspect is a scientific question, the study objective, study parameters, et cetera. Speaking to a specific scenario whereby a study may be-- potential study may be a correct fit-for-purpose study, a device may present with a situation or scenario whereby there's limited evidence or limited consensus.

CDR Kim Piermatteo: Oh, Femi.

Olufemi Babalola: Sorry?

CDR Kim Piermatteo: Sorry. Sorry. You cut out for a minute there. I lost you. Can you just jump back another sentence?

Olufemi Babalola: Sure. A device may present with a situation or scenario whereby there's limited information or no consensus on outcomes to collect as part of a clinical trial. A fit-for-purpose PPI study may adopt a best worst scaling method to inform outcome or endpoint selection by understanding the patient priorities. Thank you very much, Kim.

CDR Kim Piermatteo: Thanks, Femi. I apologize. I think that was on my end. Okay, so the next-- I see Bennett, you have your hand raised again. So Bennett, I'm going to go ahead. I'm unmuting your line. Please unmute yourself and ask your question.

Bennett Levitan: Well, thank you. So this is an issue that is probably going to become more and more important. So the guidance says you want to see the preference results. Now if you want-- do you want just a detailed report or an electronic data set? The electronic data set is going to be pretty important because right now there really aren't CDISC requirements adapted for preference methods. So how do you want the data? Just the report, or more?

CDR Kim Piermatteo: Thanks, Bennett, for that question. I'm going to just open it up-- go ahead. Sorry. Open up to any of the panelists.

David Gebben: I'll take the first cut. And Femi, if you want to jump in at any point. So again, I would say at this point, CDRH would expect if we request the actual data, it would be in a format that, like other data, would be easily manipulated with a data handbook, data dictionary, and we would also want to make sure we have the protocol so we know what pieces are there. Femi, is there anything you'd like to add?

Olufemi Babalola: Yes. Thank you, Dave. Bennett, we highly encourage early interactions with the FDA on these kind of questions. Like Dave said, the protocol, including detailed information about the study design analysis, et cetera, is very welcome. And that way, when we get to questions around the format of the data, we've already had those discussions early in the process. Thank you.

CDR Kim Piermatteo: Thank you, Femi and thank you, Dave. And thank you, again, Bennett, for the question. We have another question, and that's coming from Susanne. Susanne, I have unmuted your line. Please unmute yourself and ask your question.

Suzanne, I see that you have unmuted your line. You may be double muted.

Susanne Clinch: Can you hear me now?

CDR Kim Piermatteo: Yes, I can.

Susanne Clinch: Great. Thank you. I was wondering how much we can assume this draft CDRH guidance carries over to CDER's and CBER's thoughts on PPI as well.

CDR Kim Piermatteo: Thank you, Susanne. Does any one of the panelists want to comment on Susanne's question?

David Gebben: At this point, we are aware that CDER is working on a draft guidance. To the point of how much this will or will not impact, this covers CDRH and combination products with CBER. Beyond that, I would hesitate to comment on anything that CDER is planning or intending. Katie or Cyndi, do you wish to add anything?

Kathryn Capanna: Just a clarification as relates to CBER. This covers device led combination products that would fall under CDRH as the primary. But yes, I agree with Dave.

CDR Kim Piermatteo: Thanks, Susanne, for that question. And thank you, Dave and Katie. Okay, I'm going to make another call out. If anyone has any questions or comments that you would like to ask our panelists today regarding this draft guidance, please raise your hand in Zoom.

Okay, seeing none, I'm going to go ahead and move to close today's webinar. Wait. Shali? Shalili? You have snuck right in. I am going to go ahead and unmute your line. Please unmute yourself and ask your question for the group.

Shaili Dayal: Thank you. I thought I had raise my hands, but. But I have a quick question. So I do see that this guidance have recommendation to consider this at all stages of the device life cycle. But I was wondering, is there any specific circumstances where you think it will have the most weight in decision making? For example, if there are any specific criteria or examples where you think CDRH can directly impact approval.

CDR Kim Piermatteo: Thanks for that question. I'm going to turn it over to the team. Cyndi or Femi, did you want to start? Anyone else, feel free to chime in or add on.

Olufemi Babalola: I can chime in. Generally speaking, questions like this, we take them on a case-by-case basis. But PPI is only one part of the overall evidence package that we consider the FDA at several points for benefit risk determination. What exactly will happen, again is going to depend on a case-by-case basis. PPI doesn't necessarily replace bad clinical data. But yes, I'll stop there. It's on a case-by-case basis and it depends on the product and the device area as well.

Cynthia Grossman: Well, I'll just weigh in briefly just to agree with Femi, but also just to add that the history that Dave laid out of our efforts within a patient preference information and to advance this methodology, as Dave pointed out, really started with a focus on benefits and risk, and now we see the opportunity to expand across the total product life cycle.

So I think your question is a good one in the sense that I think time will tell in the specifics of how PPI is used and where it can play and where it has opportunity to inform regulatory decision making across the total product life cycle. But as far as sort of our examples and the work that we've done historically, it has focused more, as Dave pointed out, and it started with benefit-risk. But we really see the opportunity across the board.

CDR Kim Piermatteo: Thank you, Femi and thank you, Cyndi, for that response. And thank you, Shaili, for your question. Okay, seeing no more raised hands, I'm going to move to close today's webinar. Thank

you all for attending today and your participation. Before I get into my closing logistical remarks, I'm going to turn it back over to Dave to provide some final thoughts for today. Dave?

David Gebben: Thank you, Kim. Again, I'd like to thank everyone for joining us. As we've said, the comments are due December 5, 2024, for consideration as part of the final guidance. We do recognize that your comments, your critiques, and your suggestions are going to make a much more useful document to be able to incorporate the patient voice. So we look forward to your comments. Thank you. Kim?

CDR Kim Piermatteo: Thanks, Dave. From my end, I want to remind everyone a recording of today's webinar and a transcript will be posted in the next few weeks to the webinar event page, as well as to CDRH Learn under the section titled How to Study and Market Your Device and the subsection Cross-Cutting Premarket Policy. A screenshot of CDRH Learn, those headers, and where you can find those materials is provided on this slide.

If you have any additional general questions regarding today's webinar, please feel free to reach out to us in DICE at dice@fda.hhs.gov.

And lastly, we hope you're able to join us for a future CDRH webinar. And a listing of all of our upcoming CDRH events, including future webinars, is available via the link provided on the bottom of this slide at www.fda.gov/cdrhevents.

Thank you all again for joining us. We hope you have found today's presentation and interactions informative. This concludes our webinar. Have a nice day.

****

END