

**Principles for Selecting, Developing, Modifying, and Adapting Patient-Reported Outcome Instruments
for Use in Medical Device Evaluation - Final Guidance
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Moderator: Elias Mallis

Elias Mallis: Hello. And welcome to today's CDRH webinar. This is Elias Mallis, director of the Division of Industry and Consumer Education in CDRH's Office of Communication and Education. And I'll be your moderator for today's program.

Today's topic is on the final guidance, titled Principles for Selecting, Developing, Modifying, and Adapting Patient-Reported Outcome Instruments for Use in Medical Device Evaluation. As you'll learn more today, this final guidance serves to promote one of FDA's priorities to advance patient perspectives and the development, evaluation, and surveillance of medical devices. This final guidance has recently been published. So we're holding this webinar to provide you with an opportunity to learn more as you consider incorporating the concepts described in the guidance into the total product lifecycle of your medical devices.

It's my pleasure now to introduce you to our presenter for today's program, Dr. Fraser Bocell, psychometrician in the Patient Science and Engagement Program in CDRH's Office of Strategic Partnerships and Technology Innovation, or OST. We'll begin with the presentation by Dr. Bocell, and then come back around for a discussion and field your questions about this topic. Thank you all for joining us today. And let's hear for Fraser.

Fraser Bocell: Hello. I'm Fraser Bocell, a psychometrician and clinical outcome assessment reviewer with the Patient Science and Engagement Team at the FDA's Center for Devices and Radiological Health. Today I'm going to be sharing the new final guidance, Principles for Selecting, Developing, Modifying, and Adapting Patient-Reported Outcome Instruments for Use in Medical Device Evaluation.

I will discuss current policies that encourage the structured collection of patients' perspectives in the evaluation of medical products. I will also briefly cover the current FDA thinking around developing, modifying, selecting, and using instruments to measure the patient voice in medical device evaluation. At the end, I will leave you with some key takeaways.

Though the new guidance focuses on patient-reported outcome measures, these instruments are all types of clinical outcome assessments. Clinician-reported outcomes are based on a report that comes from a trained health-care professional after observation of a patient's health condition. Observer-reported outcomes are based on a report of observable signs, events, or behavior related to a patient's health condition by someone other than the patient or health professional.

Patient-reported outcomes are based on a report that comes directly from the patient about the patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else. And finally, performance outcomes are based on a standardized task performed by the patient.

Consider, for example, a clinical trial of an investigational device being evaluated to treat patients with chronic bronchitis. The clinicians may use a standardized scoring criteria as one way to evaluate dyspnea as part of the eligibility criteria for a trial. This is a clinician-reported outcome.

Family members may report coughing episodes or frequency of oxygen use for the study participant, which could be an observer-reported outcome. The participants may be asked as part of the trial to perform a six-minute walk test, which is a performance outcome. And lastly, patients may report on their symptoms of shortness of breath or how they are functioning in their daily life using a patient-reported outcome instrument.

I would like to start off by providing some context for the current guidance. In 2009, FDA issued a guidance on PROs, which applies to all the medical product centers. It provides recommendations about the evidence used to support a PRO instrument used in a clinical trial.

To address the 21st Century Cures Act and FDARA 2017, as well as to further the agency's efforts to include patient experience data, FDA's patient-focused drug development committed to drafting new guidance documents that clearly spell out the regulatory perspectives on the development and use of clinical outcome assessments. CDRH has been involved in the drafting of these guidance documents. The guidance series is meant to clarify the ways that stakeholders can collect patient experience data. They are intended to facilitate the advancement and use of systematic approaches to collecting and using robust and meaningful patient and caregiver input that can better inform medical product development and regulatory decision making.

This guidance series will eventually replace the final guidance on PROs issued in 2009 and will cover all types of clinical outcomes assessment. The patient-focused drug development guidance series consists of five guidances, of which four are relevant to our discussion today. The first two guidance documents of the series cover how to collect comprehensive and representative input, as well as appropriate methods to identify what is important to patients.

Guidance one was issued as final in June 2020. And guidance two was issued as draft in 2019. The last two guidances in the series will focus on how to select, develop, or modify fit-for-purpose clinical outcome assessments and then incorporate it into clinical studies. Draft guidances three and four are currently in development. While we are participating in the development of the draft guidance documents, the regulations and principles specific to CDRH, such as the least burdensome principal, led CDRH to develop and issue a guidance specific to PROs and medical devices.

The new guidance I am discussing today, principles for selecting, developing, modifying, and adapting patient-reported outcome instruments for use in medical device evaluation, or the PRO principles guidance for short, is meant to supplement existing guidances and clarify where there are areas of flexibility for medical devices.

There are three objectives highlighted in the guidance. As I go through the guidance, I'll discuss the principles to be considered, recommendations for ensuring the PRO is fit-for-purpose, and outlining some best practices for selecting, developing, modifying, or adapting PRO instruments using the least burdensome approach.

The guidance applies to PRO instruments used in medical device evaluation across the total product life cycle. As I mentioned, it supplements the resources I discussed earlier. While it communicates what the FDA believes are some best practices, it does not detail methods or steps of developing, modifying, or adapting a PRO instrument, which is addressed in other FDA guidance documents.

Here are the key principles described in the guidance. First, it's important that sponsors clearly to define the concept being measured. The concept might be pain intensity. The sponsor should be clear about how they intend for the concept to be interpreted. It is helpful if it is clear how the PRO instrument is being used in the clinical study.

Clearly illustrating how the PRO is used in the clinical study helps to define what conclusions can be drawn from the data. Sponsors should collect and present evidence that shows the instrument is fit-for-purpose. And finally, clear, effective, and appropriate communication of PRO results is critical to provide useful information that better informs health-care providers' and patients' decision making.

One point that is emphasized in the guidance is the importance of using a PRO instrument in a clinical study that is fit-for-purpose. What do we mean by fit-for-purpose? According to the glossary, it is the conclusion that the level of validation associated with the biomarker or clinical outcome assessment is sufficient to support its context of use, meaning the validity evidence should support the context of use.

This fit-for-purpose approach is meant to provide flexibility in generating the evidence used to support the PRO instrument. The concept being measured, the intended use of the PRO instrument, and its role in the protocol and statistical analysis plan will help determine the recommended level of evidence needed and flexibility in generating that evidence.

A key consideration for the context of use is assessing the population where the validity of evidence was generated. The population in which the validity evidence was gathered should be consistent with the intended use population in the clinical study protocol. This is just one step in determining whether a PRO instrument is fit-for-purpose.

There are a few best practices described in the guidance document that could be implemented to make the process of selecting or using or modifying a PRO instrument for a specific use within a clinical study more efficient. I will talk about each consideration.

While PROs may be included in clinical studies, they do not always reflect concepts that are important to patients. We encourage a focus on concepts that are relevant and impactful to patients. The guidance document details that the instrument should not only be patient focused, but also designed to be easily understood by patients and provide response options that make sense to the patients. For example, a questionnaire should avoid medical terminology that may not be familiar to the patients. One approach to accomplishing this goal is to work with patients in the development of these instruments.

Whether you're selecting or modifying an existing instrument, developing a new instrument, using a PRO instrument in a premarket study, or as part of post-market surveillance efforts, the guidance document recommends that you clearly define the role of the PRO in your protocol and statistical analysis plan. As discussed during the FDA public meeting held in December 2019, to help define endpoints in clinical studies, consider these useful resources-- the International Council for Harmonization, or ICH, guideline E9, Statistical Principles for Clinical Studies, and the Revision 1 Addendum. It may be beneficial to leverage existing appropriate instruments and the associated evidence to measure a given concept in a clinical study.

We encourage you to consider all the literature, not just the validation papers associated with a particular PRO instrument. You should provide documentation to support the validity of the PRO instrument for the proposed use in the clinical study. You may submit published articles, qualitative

research transcripts, and summaries, or other data that helps us evaluate the PRO instrument and the associated scores.

If after looking for an existing instrument, you discover that you need to create a new PRO instrument, we encourage you to consider efficient development approaches. For example, you may want to use alternative platforms or work with other interested parties during the development process. PRO instruments are increasingly incorporated into clinical practice, along with ongoing efforts to develop coordinated registry networks to help generate real-world data.

Developers could explore generating validity evidence, including translations, by collecting the evidence during the conduct of ongoing studies, as well as during the planned development cycles of a device. Such an approach of using parallel development work on the PRO and device may be more efficient. Additionally, collaborations allow for pooling of resources, not only financially, but also in terms of access to expertise and key stakeholders, such as patients. The collaboration projects could lead to a PRO instrument that could benefit many interested stakeholders.

Finally, I've listed a few resources based on the topics discussed today. If you are a PRO instrument developer or a new user, the 2009 FDA PRO guidance is a good resource, as well as this new guidance. I've provided links to the two final guidances discussed today, the 2009 PRO guidance and the newly finalized principles guidance.

If you're looking for where to start or just want to find out more information, I would recommend you visit the CDRH COA website as a starting point. It contains a report about the PRO use in medical device submissions, case studies describing the use of COAs, including PROs, FDA research efforts, as well as other resources. And if you are interested in where things are headed, I suggest you visit the website for additional information on the Patient-Focused Drug Development Guidance Series.

If you have questions for us, you can contact us at the CDRH-PRO mailbox.

In conclusion, I want to emphasize a few points. The newly final guidance complements the current 2009 PRO guidance, as well as the PFDD guidances under development. The key principles outlined help us understand and evaluate how a PRO instrument is being used. The best practices outlined in the final guidance document are meant to ensure relevant, reliable, and sufficiently robust PRO instruments are developed, modified, and adapted using a least burdensome approach.

And, as always, the use of PRO instruments is voluntary if other means of measuring the concept of interest exists. Thank you. And we will now transition to answering any questions.

Elias Mallis: Thank you, Fraser. This was a great overview for our audience today. I look forward to our next segment now, which is our Q&A segment of the program. But first, I'd like to also introduce our FDA discussion panel, who will join Fraser in answering your questions. First, Dr. Michelle Tarver, Deputy Office Director in the Office of Strategic Partnerships and Technology Innovation, OST, and Katie Capanna, Deputy Director in OST's Division of All Hands Response, Science, and Strategic Partnerships, or DARSS.

So let's review how we'll manage this segment. To ask a question, please click the Raise Hand button, which should appear on the bottom of your Zoom screen. I'll announce your name and then I'll invite

you to ask your question. You'll see a prompt on your Zoom screen. To speak, please acknowledge the prompt and then go ahead and ask your question.

Now, a few more tips-- please limit yourself to one question at a time. And try to keep it as short as possible. And number two, please refrain from asking any specific submissions or data-specific questions. For these really detailed questions, we'd ask you to consider submitting a Q-Submission or reaching out to the team offline. Fraser shared the email address a few slides back, in his presentation. After you ask your question, please lower your hand. And if you have more questions, no problem at all, just go ahead and raise your hand again. And we'll come back to you if we have time.

Now, as we wait to hear from some of you from some of your questions, I'd like to welcome our newest panelists with a few questions that we've gotten over the past few weeks about the guidance.

So our first question will go to Michelle first. Michelle, thank you for joining our panel today. Here's our first question for you. How does the PRO guidance further the FDA's efforts around patient science and engagement?

Michelle Tarver: Thank you very much for the question. Well, FDA's Patient Science and Engagement Program really aims to proactively integrate the patient's perspective on what it's like to live with their health condition and its treatment and management of that condition. And it integrates that into the total product lifecycle of medical devices. Our ultimate goal, as you already know, is to help protect and promote public health. And these instruments are a way for us to understand how patients feel and function and survive and use that information collected in a structured way so that we can make valid scientific inferences.

This can be very helpful in our regulatory and health-care decision making. And this guidance is really designed to help stakeholders understand those principles as best practices that can help in the development and use of PRO instruments in a way that is least burdensome and can augment their medical device development portfolio.

Elias Mallis: Thank you, Michelle. And thank you for joining our panel today. Let's hit our next question and invite Katie to join us for the response.

So for this second question, the guidance discusses the importance of ensuring that PRO instruments are, quote unquote, fit-for-use. Can you clarify a little bit more what this means?

Katie Capanna: Yes, and thank you, Elias, and thanks to everyone for joining us today. This is a really important concept for patient-reported outcomes and other tools that we use to gather evidence and support of regulatory applications. For PRO instruments, there are many different ways they can be used across the total product life cycle. And the type of evidence that FDA would expect to see or that the sponsors would need to gather will depend on how the instrument is planned to be used.

And so, for example, a patient-reported outcome instrument could be used to assess whether or not a patient fits the eligibility criteria to participate in the study. Commonly they are used to measure primary or secondary endpoints, either as a standalone or frequently as part of a composite endpoint that might include some of the other types of assessments that Fraser mentioned. It could also be used in post-market studies, or registries that are collecting long-term longitudinal data on the performance and safety and effectiveness of devices.

And so depending on how the instrument is planned to be used, FDA would consider what type of evidence would be needed to support that. And we refer to this approach, which is really flexible and tuned to the purpose, as fit-for-purpose.

Elias Mallis: Thank you, Katie. Thank you for joining us. Alright, let's get to our first caller. So, Sethu, I am unmuting you. Please go ahead. And welcome to our webinar. And go ahead and ask your question for our panel today. Alright, Sethu, are you with us? And go and proceed with your question.

Alright, we're going to-- I'm going to mute you again. And we'll try to come back to you in a couple of minutes.

William, let's go to you next. Go ahead and unmute yourself. And go ahead and ask your question.

William Zhou: Ah, thank you. I have one question. For this burdensome design, if I took a current four existing survey PRO that has been validated and picked three of the most relevant questions from the four PROs and the construct into a new PRO, will that new PRO need to be validated clinically first before use? Or I can use the existing validation from the earlier four PROs as a support?

Elias Mallis: Yes, thank you for that question. Fraser, may I ask for you to provide a response?

Fraser Bocell: Yes, thank you for that question. That's a really interesting, good question. The idea here is it's partially going to depend on how you're using it. If you're generating a new score based on those items, what you're doing is you're creating a new score that's different from the previous scores that have all the existing validity evidence on them. And so we might actually need some additional validity evidence to help us interpret that new score that's been developed.

But if it's something that you're using the individual items descriptively, we may be able to rely on some of the existing evidence that exists and move forward with that. So it's going to depend on the exact situation that you're using. But in most cases, we try to leverage the existing validity evidence as best we can.

William Zhou: Thank you.

Elias Mallis: William, did that answer your question?

William Zhou: Yeah, what I heard is if the score, for example, 1 to 10 scale, 1 to 5 scale quantitatively may need new validity evidence. If the survey is just descriptive, like a binary decision, could be allowed.

Fraser Bocell: Yeah, I think what I mean is so if you're taking-- if initially you had a scale of eight items and you're only using four of those and creating a sum score based on those four items instead of a sum score based on the eight items, because we're changing how that score is calculated, what items are based on, we might need an additional evidence of that. So that's where we have to look at the changes that were made.

William Zhou: OK, thank you.

Elias Mallis: William, thank you for joining us. And thank you for that question. Bobbi, I'm going to go to you next. I'm going to unmute you. So go ahead and ask your question.

Bobbi Ohumukini: Can you hear me?

Elias Mallis: You sound great. Yes. Welcome, thanks for joining us.

Bobbi Ohumukini: I was just wondering if the slides were available after the webinar.

Elias Mallis: The answer is yes. And actually, I don't know how you found the Zoom link, but we actually posted the slides on the webinar page.

Bobbi Ohumukini: Oh, OK.

Elias Mallis: So they were on the page where we promoted the webinar. And also we posted the slides already on CDRH Learn. I'm going to, at the end of the presentation, of our session today, I'll show where that's going to be located. And also, after this program, we're going to post a copy of this recording, as well as the transcript, within a couple of weeks.

Bobbi Ohumukini: Wonderful. Thank you.

Elias Mallis: OK, did you have any specific questions for the panel? Alright. Thank you for joining us. We'll continue with Melinda. I'm going to unmute you next so you can join us with your questions. So thank you.

Melinda De Jesus: Hi. Good morning. And go ahead and ask your question.

Melinda De Jesus: Can you hear me OK?

Elias Mallis: You sound great. Thank you for joining us.

Melinda De Jesus: Great. I was just wondering what the FDA's position is or if you could speak more to the topic of validated questionnaires in other languages and how that can be either leveraged or what is the FDA's position in terms of utilizing other language questionnaires?

Fraser Bocell: Yeah, no, that's an excellent question, especially as we move into or as we continue to be in multinational programs. One thing we really look at is looking at the patient population and is the patient population appropriate? And are there cultural differences or other differences that might affect what we're looking at?

And so really making sure that we can translate the content in a way that is appropriate for whichever population it was developed in, whatever language it was developed in, and then also make sure that that's also appropriate for the new population. So that's not only the translation, but the potential for cultural adaptation. And so that's something we look at.

And I think one of the things we make clear in the guidance is that we're very open to looking at all the available validity evidence that's out there. And if some of that evidence is coming from other populations, other languages, that's something we'll take in to consider. And we'll look at the evidence

of whether that is applicable to the indication for use population that we're going to be studying in the clinical study.

Melinda De Jesus: Thank you.

Elias Mallis: Thank you, Melinda, for the question. Thank you, Fraser, for answering it. We'll keep going. Again, please raise your hand if you have a question for our panel. While we're waiting for more questions, let me send another one to you, Fraser, to address that we've gotten in the past couple of weeks.

The guidance states that the strength of evidence needed to support the measurement properties of a PRO instrument can depend on the role of the instrument in the clinical study protocol and statistical analysis plan. For example, you mentioned a PRO instrument used as a secondary endpoint would need different evidence than if it were used as a descriptive safety assessment. Can you elaborate more on this?

Fraser Bocell: Yeah, I'd be happy to. This is a question that's near and dear to me. We really recommend that you think about the conclusions that you want to be drawn from the data. So in a device with known risks, a PRO instrument could be used descriptively to evaluate and inform patients on the rates of symptoms they would expect after treatment. We'd want to know that the patients understand and can respond appropriately and that the correct symptoms and the aspects of the symptoms are measured.

Finally, those descriptive results should be easy to interpret if we're going to include them in the SSED or other labeling. So on the other hand, if we're using as a PRO instrument as a secondary endpoint in the statistical analysis plan, we start to need more information on its statistical and psychometric properties. This way, we can have more confidence in any conclusions we're going to draw from that data. So we can always use the Pre-Submission, or you can always use the Pre-Submission process to come and discuss any questions you may have regarding that specific situation.

Elias Mallis: Alright, thank you. Thank you so much. Kendal, let's go to you with our next question for the panel. Please go ahead and unmute yourself and share your question.

Kendal Whitlock: Thank you so much. The question really is about the FDA's thinking about points of entry for patients into the participation in the development of PROs. I often get the question of whether or not smart speakers, for example, is something that a patient who may know how to use a smart speaker would readily use. And I wonder if the FDA has any thinking on not only that as an example of a simple point of entry into participation, but more broadly speaking, how patients might find out about opportunities to learn where they can contribute their points of view so that there is further evidence of the patient's preference or what their experience of their managing of their disease is for the use of or the development of a PRO. Thank you.

Elias Mallis: Alright, thank you for that question. I'll turn it back to our panel to provide a response. Fraser, would you like to take the first stab at responding?

Fraser Bocell: Actually, it looked like Michelle was about to unmute herself. So I'll give her the opportunity to answer that one if she would like.

Michelle Tarver: Thanks, [INAUDIBLE]. I'm happy to answer it. Thank you for the question, Kendal. I think you bring up the opportunity for digital health technologies to potentially expand the ability for patients to participate in many aspects of medical research, including patient-reported outcome tool development.

I think it's an interesting concept. And it's something that we are exploring, ways in which we can bring more patients from various communities into the development process.

In terms of-- we have, obviously, during COVID-19 public health emergency, we've had to leverage remote approaches to bringing different patient perspectives into tool development. And we've seen that work quite effectively. So we are very much open to exploring other opportunities. So thank you for that question.

Kendal Whitlock: Thank you so much, Michelle.

Elias Mallis: Thank you, Michelle. Let's get to another question that's come in over the last few weeks. Back to you, Fraser. Can I collect PRO validation evidence during a pivotal study to support the use of a PRO in that same pivotal study?

Fraser Bocell: So really, whenever possible, we recommend that you use early feasibility, a phased clinical study, or alternative platforms for generating validity evidence. In general, the same data cannot be used to both support the interpretation and draw conclusions in a clinical study. So really, we would recommend that the validity evidence should support the use and-- so the validity evidence should support the use and interpretation of the PRO instrument scores. And we would really recommend that you collect that evidence separately from the evidence that you're going to use to support the clearance or approval of your device.

Elias Mallis: Alright, thank you so much. Let's get to another question. The guidance encourages collaborations in the precompetitive space. Can you speak a little bit more about this?

Fraser Bocell: Yeah, and I think this somewhat relates back to the question from the audience a couple of times ago, where we think that collaborations are a good way to tap into expertise that you may not have available internally, such as experts in PRO development, patient groups, or health professional organizations. So we really recognize that these collaborative approaches can be challenging. But we believe that they present an opportunity to benefit from the shared resources, as well as to be able to better collect information in a balanced manner and really involve patients in the development processes.

Elias Mallis: Alright, thank you so much. Again, this is a chance for your questions for our illustrious panel. Don't be shy and go and ask them. We'll keep going with more questions we've gotten. So back to you, Fraser. Does this guidance apply to other types of clinical outcome assessments, such as performance outcomes?

Fraser Bocell: So this guidance is really specific to patient-reported outcome instruments. But we do feel that some of the best practices highlighted are likely applicable to other COAs. So we'll note that when the PFDD guidance 3 and 4 publishes final, they will both cover all types of COA. And so until then, we welcome discussions through the Pre-Submission Program or other avenues on how the principles highlighted in the guidance may apply to your particular circumstances.

Elias Mallis: Alright, thank you very much. Melinda, we'll come back to you if you have another question to join and ask for our panel.

Melinda De Jesus: Thank you. I'd like to follow up with the gentleman on his comment about how the strength of the evidence can support the PRO interpretation and talk a little-- I was hoping you'd talk a little bit more about the use of the PRO in descriptive safety and thinking about the conclusions that you can provide as context for risk for the device. And I was hoping you could speak a little bit more to that.

Fraser Bocell: Yeah, I think I can say a couple extra words. And then I might open it up and see if any of my other colleagues want to say anything. But the example that I provided in terms of symptoms and the device where we know the risks, we consider that to be additional information that is informative to both patients and caregivers and care professionals in making their decisions about that device.

But if we're moving up in the importance of that and the patient-reported information becomes part of the key safety considerations of the device, if we're really putting a lot more faith and a lot more-- if we're really having to rely on that information a lot more in terms of the safety of the device, then we might need a little bit more information in terms of the conclusions that we can draw from that data. So if we move beyond it being descriptive and generally informative of what can be expected to more part of the primary decision on the safety of the device, we might need more information regarding the properties of that data.

Michelle Tarver: And if I could just add a little bit to that, I mean, I think this comes back to the point that Dr. Bocell mentioned early on, which is the fit-for-purpose. It depends on how that instrument is being used. Sometimes it's descriptive data only because it is an ancillary endpoint. But if it is an endpoint of the study or it is a performance goal, then that is going to maybe require some additional evidence.

So it really does depend on how it's being used, what concept it's measuring, and the best approach to measuring that concept. And I think those specific, we can't give a general yes or no answer to that. And that's really one of those topics that we really encourage you to reach out to the review offices and bring that particular question up. Our team is happy to join in those conversations as well.

Melinda De Jesus: Thank you. And then when you say performance goal, are you referring more towards-- is that meaning labeling claims? Is that what that's meant to mean?

Michelle Tarver: If it's meant to mean anything, that potentially could be in the label, but also part of the regulatory decision-making process. So for any information that would be considered the evidence that would be informing our regulatory decision. It could be either.

Elias Mallis: Melinda, thank you for joining us and for your question. Let's keep going with our next question. LYBL, I'm going to unmute you now. Please go ahead and unmute yourself and ask your question of our panel.

LYBL: Thank you. So my question goes, if the PRO has to be in the language that's the participant's native language, or if it can be in English if the participants understand English.

Fraser Bocell: That's a good question. And part of that would actually go down to your inclusion criteria. And I know that something like that can actually make it easier to pool the data and look at the data. And I think that's something that we'd have to look at and make sure that it's appropriate. But if you can make the case that according to your inclusion criteria of say, that they need to be able to speak and read and respond in English, that would be something that we would definitely would be open to.

LYBL: Thanks.

Elias Mallis: Alright, thank you for the question. Thanks for the answer. Let's get to another written question that we've gotten in advance. Back to you, Fraser, what is the relationship between this guidance and the patient-focused drug development guidances?

Fraser Bocell: So yea, I think that's a great question. That's one we want to make clear, is that this guidance is really meant to supplement the current 2009 PRO guidance. And then in the PFDD guidance series, when finalized, that's series is going to replace the 2009 PRO guidance. And so we think the principles for PRO guidance will continue to supplement those PFDD guidances when they're final, and then by highlighting some of the best practices using the least burdensome approach, which is really particularly relevant to medical devices.

Elias Mallis: Alright, thank you very much. A lot of activity in this space across the FDA, so thank you for explaining that. Let's get back to another caller, Beluh. I'm unmuting you now. You're welcome to share your question with our panel.

Beluh Mabasa: Maybe my question is very simple. I want to know, is SOTA, state-of-the-art, part of the patient-reported outcome also? Why [INAUDIBLE] talking about SOTA? Thank you.

Fraser Bocell: I'm sorry, could you repeat the question? I'm not sure I caught all of it.

Beluh Mabasa: Yeah my question is how about SOTA? SOTA is state-of-the-art. This state of the art can include the patient-reported outcome also. Hello?

Elias Mallis: Thank you for the question. For our panel, I don't know if that's a question we would request be submitted as an email. And then we can follow up offline.

Beluh Mabasa: OK. OK.

Elias Mallis: Yes. Fraser had listed his email address. Go ahead and email us and then we can take a look at that question and then follow up with you individually.

Beluh Mabasa: Yeah, I think, sorry, I want to know why this guidance not discuss or address about the state-of-the-art.

Michelle Tarver: So I think, if I think I'm understanding your question correctly, you're asking about the state-of-the-art methodological approaches that could be used in patient-reported outcome development? Is that what you're asking?

Beluh Mabasa: I am very sorry. I have read the guidance, the draft of the guidance. But the guidance is not talking about the state of art.

Michelle Tarver: So I think if you're talking about the methodological approaches and the ways in which people can analyze or develop patient-reported outcomes, those details are in other guidance documents that Dr. Bocell alluded to and will be in-- they were discussed at some of the public meetings as part of the patient-focused drug development guidance series. If you're asking about a different question, we are going to ask that you send it by email, because I don't think we're understanding the nuance that you're alluding to. So an email might be very helpful.

Beluh Mabasa: OK. OK. I will write by email. Thank you very much—

Michelle Tarver: Thank you.

Beluh Mabasa: --for the information. You're welcome.

Elias Mallis: Beluh, thank you for joining us and your question. Michelle, thank you for the response. Thank you so much.

Beluh Mabasa: You're welcome.

Elias Mallis: Thank you for joining this webinar. So with that, I think we have come to the end of our question-and-answer segment. So I will turn it back to Fraser for your final thoughts for our audience today.

Fraser Bocell: So yeah, thank you everybody for joining us. We hope that the presentation and the question-and-answer session today have been helpful to you. Likewise, we hope this new guidance clarifies some of our current thinking and provides some flexibility in measuring and including the patient's voice in the total product lifecycle of medical devices.

We've covered the key principles as well as considerations for ensuring that the PRO instrument is fit-for-purpose. We also looked at some of the best practices that may be helpful for a least burdensome approach to selecting, developing, modifying, or adapting a patient-reported outcome. And finally, we pointed out some of the different resources, including our website and email address, that are available for questions or further information.

So, once again, I want to thank you for joining us today. And I will pass it back to my colleague, Elias.

Elias Mallis: Thank you so much. And with that, this concludes today's webinar. I'd like to thank our panelists, Doctors Fraser Bocell and Michelle Tarver, as well as Katie Capanna for our discussion on the use of patient-reported outcome instruments for medical devices. My thanks to you, our audience, for your participation and your great questions today.

As I noted earlier, a recording of today's webinar and presentation, as well as a transcript, will be posted to CDRH Learn in a few weeks. Please visit CDRH Learn at the link shown on this slide. And the topic will be placed under the section Specialty Technical Topics under the new subsection we've labeled Patient Engagement. We have some growing efforts in this space. So please look for all related efforts involving patient engagement here.

For additional questions about today's presentation, you can email us at our division at DICE@fda.hhs.gov. We always appreciate your feedback about the webinar series and encourage you to complete a brief survey that you can find at the link shown here on the slide.

And finally, the bottom link here lists upcoming webinars. And we're very pleased to share with you that we have another topic on patient engagement coming up on March 22. So if you have an interest in that topic, please join us then.

Again, this is Elias Mallis. Thanks for joining us today. Take care and we will see you next time.

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