CDRH's New Draft Guidances to Continue to Modernize the 510(k) Program
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Moderator: CDR Kim Piermatteo

CDR Kim Piermatteo: Hello and thanks for joining us for today's CDRH webinar. 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 in CDRH's Office of Communication and Education. And I'll be your moderator for today.

We are holding this webinar to describe the FDA's ongoing efforts to modernize the premarket notification or 510(k) Program, including providing an overview of three new draft guidance, which were issued on September 7, 2023, that focus on best practices for selecting a predicate device, recommendations for when clinical data may be necessary in a 510(k) submission, and evidentiary expectations for 510(k) implant device submissions. Today, we will also respond to your questions.

Before we begin, I'd like to provide two reminders. First, please make sure you've joined us through the Zoom app and not through a web browser to avoid technical issues. And 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.

I now have the pleasure of introducing our presenters for today's webinar. Megha Reddy, Regulatory Advisor on the Regulatory Policy and Guidance staff within the Office of Product Evaluation and Quality, or OPEQ in CDRH; Dr. Mary Wen, Deputy Director for the Division of Submission Support within OPEQ in CDRH; and Dr. Peter Yang, De Novo Program Lead within the Division of Submission Support in OPEQ in CDRH as well.

We'll begin with a presentation from our presenters and then field your questions about our topic. Thank you all again for joining us, I'll now turn it over to Megha to start today's presentation. Megha.

Megha Reddy: Thank you, Kim. Today, we are here to talk about our recent efforts to strengthen and modernize the 510(k) Program. We will touch on this continuing effort, as well as the content of these three new draft guidances. These new draft guidances are intended to modernize the 510(k) Program, to address the increasing complexity of, and to advance the safety and effectiveness of medical devices.

The draft guidances are Best Practices for Selecting a Predicate Device to Support a 510(k) Submission, Recommendations for the Use of Clinical Data in 510(k) Submissions, and Evidentiary Expectations for 510(k) Implant Devices. While we will discuss the current policies in these draft guidances today, we'd like to note that these are draft guidances and are not for implementation. We are seeking your feedback on these draft guidances before the comment period closes on December 6th, so that we can consider your comments as we begin to work on the final guidances. Now let's dive in.

Over the past decade, CDRH has continually worked to strengthen and modernize the 510(k) Program. It began over 10 years ago starting with the evaluation and set of recommendations for improvements to the 510(k) Program. After that, in conjunction with the recommendations, we began working on a number of actions that we could take to provide more transparency and clarity on the 510(k) process.

For example, in 2014, we issued a guidance on the 510(k) Program evaluating substantial equivalence in 510(k)s, also referred to as the 510(k) Program guidance, which provided needed transparency on the decision-making process that we use to determine substantial equivalence. Since 2009, CDRH has issued more than 100 final crosscutting and device-specific guidances to provide clarity on areas of 510(k) review.

In 2018, we published the Medical Device Safety Action Plan, which outlined a vision for how CDRH can continue to improve our programs and processes to assure the safety of medical devices throughout the total product life cycle, to identify and resolve safety issues, and to advance innovative technologies that are safer and more effective.

In alignment with the Medical Device Safety Action Plan and, more specifically, to continue to improve the 510(k) Program and to advance innovative technologies that are safer and more effective, we opened a docket in 2019 and encouraged the public to give us feedback on a proposal to strengthen the 510(k) Program. This proposal included posting on our website a list of 510(k)-cleared devices that demonstrated substantial equivalence to older predicate devices, encouraging manufacturers to use more modern predicates instead.

It also encouraged the public to provide feedback on other actions that we could take to promote development of safer, more effective devices, including recommending actions that may require new authority, such as making some older devices ineligible as predicates. We received a number of comments in the docket that spurred the development of these three new draft guidances to improve the 510(k) Program, starting with a proposal to post on our website a list of FDA-cleared devices that demonstrated substantial equivalence to older predicate devices. We heard from the feedback submitted to the docket that this may not be the best way to promote safer and more effective devices.

For example, certain implant devices may have a long history of safe use. This prompted us to rethink the question and instead focus on utilizing best practices when selecting a predicate device rather than solely focusing on the age of a predicate device. These best practices are described in one of our new draft guidances. We also heard from the feedback submitted to the docket that guidance would be helpful on certain complex topics, including the use of clinical data in 510(k) submissions and recommendations for 510(k) implants. These topic areas are the subject matter of the other two draft guidances.

Today, we'll dive into the content of these new draft guidances and address how, when finalized, these guidances may help improve the predictability, consistency, and transparency of the 510(k) Program. We'll also explain how these new draft guidances are consistent with the 510(k) Program guidance. In particular, when finalized, these guidances are intended to be used in conjunction with the 510(k) Program guidance and may help with certain topics for your 510(k) submission.

None of these guidances are intended to propose any changes to the applicable statutory and regulatory standards, as such, how FDA evaluates substantial equivalence or the applicable requirements, including 510(k) content requirements. Finally, we'll explain the current policies in the three draft guidances. We'll discuss the four proposed best practices for selecting a predicate device to support a 510(k) and how to use the best practices in selecting your predicate and in preparing your 510(k) submission. We'll discuss the four scenarios for when clinical data may be needed to demonstrate substantial equivalence in your

510(k) submission, some of which were initially described in the 510(k) Program guidance and are expanded and clarified in this new draft guidance.

Lastly, we'll discuss the proposed recommendations for 510(k) implant devices, which serves as a general resource in the design of appropriate performance testing for these devices and recommend the appropriate content and labeling information to include in 510(k) submissions for implant devices.

I will begin with the first of three draft guidances, the Best Practices for Selecting a Predicate Device to Support a 510(k) Submission. As I mentioned earlier, this guidance is intended to guide 510(k) submitters, who I will refer to as you throughout this presentation, through the best practices in selecting a predicate device for a 510(k) submission. It is intended to be used while preparing a 510(k) submission to help identify potential predicate devices to support substantial equivalence of the subject device to a legally marketed device. And it's intended to be used in conjunction with the 510(k) Program guidance.

We developed this guidance to promote the predictability, consistency, and transparency of the 510(k) premarket review process and so believe that the use of these best practices will help encourage the evolution of safer and more effective medical devices in the 510(k) Program. We believe that these best practices will encourage submitters, or you, to consider the characteristics of a predicate device rather than focusing on the age of a predicate alone.

When considering the selection of predicate devices during 510(k) submission preparation, we recommend that you first consider the list of all legally marketed devices. Then we recommend narrowing down this list to those devices that have the same intended use as the subject device, and any differences in technological characteristics do not raise new questions of safety and effectiveness. These are considered the valid predicate devices in the draft guidance.

Then we recommend using the best practices outlined in this guidance document to narrow this list of valid predicate devices. These best practices should be used in conjunction with the 510(k) Program guidance to determine the predicate device that will ultimately be used to support the 510(k) submission.

These are the four best practices we recommend you consider when selecting a predicate device. I will go into detail on each of these during the next few slides.

The first best practice to consider is to select a valid predicate device that was cleared using well-established methods. These methods include those from a current FDA recognized voluntary consensus standard, an FDA guidance document, a qualified medical device development tool, or a widely available and accepted method published in the public domain or in scientific literature for the context of use or that has been found acceptable through the submitter's own previous premarket submission.

We recommend prioritizing predicate devices with methods developed within a consensus environment and those that have been subject to public comment or peer review. When selecting a valid predicate device, submitters should consider how much information is available regarding the test methods used to support the predicate devices' 510(k) clearance and whether those methods continue to be appropriate for evaluating the subject device. Once you've identified a list of valid predicate devices, we

recommend conducting a search of the nonclinical tests submitted, referenced, or relied on in the 510(k) submission of the predicate to support a determination of substantial equivalence.

The second-best practice to consider is to select a valid predicate device that continues to perform safely and as intended by the manufacturer during use in its intended environment of use whenever possible. As such, we recommend selecting a valid predicate device after considering how any reported device-related adverse events, malfunctions, or deaths may have a role in the safety and effectiveness of the device.

New information about how a device's safety and/or effectiveness, including unanticipated adverse events, may become available once the device is more widely distributed and used commercially. Also, subsequent changes made to the device, including material changes or its manufacturing process, may lead to unanticipated effects that cannot be comprehensively captured during the premarket review. This new information may include, but is not limited to, a newly recognized type of adverse events associated with a medical device, an increase in severity or frequency of a known adverse event, new product-product interactions, or device malfunctions. Once you've identified a list of valid predicate devices, we recommend conducting a search for any reported injury, deaths, or malfunctions using the databases listed on this slide.

The third-best practice to consider is to select a valid predicate device that does not have unmitigated use or design-related safety issues, including consideration of emergent signals or safety communications. New information about a device's safety and/or effectiveness can become available once the device has been widely distributed and used. And this information could represent a signal that may include information related to the device malfunctions or patient injuries potentially related to improper devices or design.

An emerging signal is new information about a device that supports a new causal association or a new aspect of a known association between a device and an adverse event or a set of adverse events and for which FDA has conducted an initial evaluation and determined that the information has the potential to impact patient management decisions and/or the known benefit-risk profile of the device. Once you've identified a list of valid predicate devices, we recommend that you conduct a search of the medical device safety and CBER safety site databases to assess whether any of the valid predicate devices have an associated use-related or design-related safety issue and, when possible, to select a valid predicate device that does not have any such related issues.

Lastly, we recommend selecting a valid predicate device that has not been subject to a design-related recall. Recalls are typically voluntary actions taken by a manufacturer or may be requested by FDA to correct or improve a violative product from the market. Recalls can occur due to design defects, manufacturing defects, or labeling defects.

Design-related recalls can indicate a flaw with the design of the device as cleared and commercially distributed. Design controls under 21 CFR 820.30 include a framework that requires manufacturers subject to these requirements to establish and maintain procedures to control the design of the device in order to ensure that specified design requirements are met. When a design-related recall has been conducted for a device, adequate design control procedures may not have been implemented through the design process. In some instances, the underlying root cause of the design-related issues identified

as part of the design-related recall may not be available or a correction of these design-related issues may not be possible.

Once you've identified a list of valid predicate devices, we recommend conducting a search of the medical device recalls database to assess whether any of the valid predicate devices have an associated recall. We consider it a best practice to select a valid predicate device that is not associated with a design-related recall, whenever possible.

The 510(k) Summary is a document that provides a summary of the information with respect to safety and effectiveness of a device. It must include all the elements identified in 21 CFR 807.92. As part of our efforts to improve transparency of predicate devices, we recommend that you include a summary narrative explaining your selection of the predicate device used in support of the 510(k) submission, in the draft 510(k) Summary. Within this narrative, we recommend you include a discussion of how the best practices were used to select the predicate device proposed for use in the 510(k) submission.

This recommendation is intended to promote transparency to the public regarding the process of selecting a predicate device when using these best practices. If a valid predicate device that is consistent with any of the best practices discussed in the guidance cannot be identified, we recommend that you include a statement in the 510(k) Summary that a valid predicate device consistent with the best practices was not available. We also recommend that you use the performance data section of the 510(k) Summary to describe the ways in which performance testing was conducted to address any known safety or effectiveness concerns with the predicate device that is used to support the 510(k) submission.

Let's walk through an example together. In this scenario, a submitter is preparing a 510(k) submission for a bone sonometer and has identified only one valid predicate. This valid predicate used FDA-recognized consensus standards, has the expected frequency of reported adverse events, has no unmitigated use-related or design-related safety issues, but it has been associated with a design-related recall. So, what are our options in this situation?

In the 510(k) Summary, the submitter will reference the valid predicate device and will include a statement that it was the only available valid predicate device that could be identified. If there are multiple valid predicate devices, the submitter will also include a detailed description of the selection process for selecting the valid predicate device in addition to a rationale for why the valid predicate was selected. We recommend that the description of the selection process be in tabular format as suggested in the guidance document. Then, in the performance testing section, in addition to the standard requirements for a 510(k) submission, as outlined in the 510(k) Program guidance, the submitter will describe how the testing conducted would mitigate the safety concerns relevant to the design-related recall. In the 510(k) Summary, the submitter will include a summary of the same information that I just described.

In summary, this draft guidance outlines four best practices to consider when selecting a predicate. This guidance was developed to improve the predictability, consistency, and transparency of the 510(k) premarket review process. And we believe that the use of these best practices will help encourage the evolution of safer and more effective medical devices in the 510(k) Program. I will now hand it over to Dr. Wen, who will discuss the next guidance on the use of clinical data in 510(k) submissions.

Mary Wen: Thank you, Megha. The second draft 510(k) modernization guidance is entitled Recommendations for the Use of Clinical Data in Premarket Notification Submissions. As its name suggests, this draft guidance provides recommendations for when clinical data may be needed in a 510(k) to demonstrate that a new device is substantially equivalent to a predicate.

The 2014 510(k) Program guidance had a section on requests for performance data that identified, at a high level, the most common scenarios in which clinical data may be requested but said that list wasn't exhaustive. The recommendations in this draft guidance are consistent with the 510(k) Program guidance but expand upon that. Specifically, this draft guidance clarifies and provides additional context for situations when clinical data may be necessary. This draft guidance also provides several examples, both for when clinical data may be needed, as well as when clinical data may not be needed, to demonstrate substantial equivalence.

First, the draft guidance provides a quick reminder of when clinical data is typically reviewed in a 510(k). The figure on the right is the 510(k) Decision-Making Flowchart from Appendix A of the 510(k) Program guidance. As initially described in that guidance, clinical data may be used at multiple points in the flowchart. Under this flowchart, clinical data is typically reviewed at decision point five during evaluation of performance data, after we find that the intended use of the new device and predicate are the same, and after we find that the different technological characteristics of the devices do not raise different questions of safety and effectiveness. When clinical data is reviewed at decision point five, that clinical data is often used to determine whether the new device is as safe and effective as the predicate. This is, by far, the most common use of clinical data in a 510(k).

While much rarer, FDA may also rely upon clinical data at decision point two in the 510(k) flowchart during evaluation of the intended use. Specifically, the 510(k) Program guidance states that FDA may rely upon clinical data to determine that new or modified indications for use fall within the same intended use as a predicate device.

This draft guidance focuses on the more common scenarios where clinical data may be necessary to determine substantial equivalence, which is generally during review of performance data at decision point five.

Next, this draft guidance outlines four scenarios when clinical data may be necessary to determine substantial equivalence. The first is when there are differences between the indications for use of the new device and the predicate. The second is when there are differences between the technological characteristics of the new device and the predicate. The third is when substantial equivalence cannot be determined by nonclinical testing. And the fourth is when there is a newly identified or increased risk for the predicate. I will go into each of these in greater detail during the next few slides.

The first scenario is when there are differences between the indications for use of the new device and the predicate. As described in the 510(k) Program guidance, when the indications for use of a new device and predicate device differ, FDA must evaluate whether the indications for use of the new device fall within the same intended use as that of the predicate. FDA determines the indications for use of the new device based on the proposed labeling and the indications for use statement in a 510(k). Following review of the proposed labeling and indications for use statement, FDA may rely upon other clinical and/or scientific information submitted with the 510(k) in order to determine if the new device has the same intended use as the predicate.

When there are differences between the indications for use of the new device and the predicate, FDA recommends considering the following factors in determining whether clinical data may be necessary to demonstrate substantial equivalence. These factors are, if there are differences in the patient population, disease, anatomical site, structure, or pathology; the general to specific considerations as described in FDA's guidance entitled general/specific intended use; expansion of the device's indications for use; an unknown or different benefit-risk profile for the proposed indications for use compared to the predicate.

I wanted to highlight a couple of examples from the draft guidance, one where clinical data may be needed and one where clinical data may not be needed to demonstrate substantial equivalence. In both of these examples, there is a clear device that is indicated for use in a specific anatomic location. And the manufacturer seeks to change or expand the indications to a different anatomic location resulting in a different benefit-risk profile.

In the first example, the cleared device is already indicated for use near critical organs and use of the device in the new anatomic location actually poses less risk than the original location. In this situation, it is determined that nonclinical data may suffice to demonstrate SE due to the lower risk profile.
In the second example, the use of a device in a new anatomic location poses a higher risk because the procedure needed for the new location is technically complex. Due to the increased risk profile, it is determined that clinical data may be needed to demonstrate substantial equivalence.

The second scenario is when there are differences between the technological characteristics of a new device and the predicate. When there are differences in technological characteristics, FDA recommends considering the following factors in determining when clinical data may be needed to demonstrate substantial equivalence. These factors are, if there is a significant change in materials, device design, energy source, or other device features.

As an example, let's say a manufacturer wants to add additional sizes of an implanted device to its existing line of cleared implanted devices. In this situation, the change in technological characteristic is in size. No other changes are made to the design materials or other device features.

In the first example, if the new sizes are within the minimum and maximum of the already cleared implanted devices, it's unlikely that clinical data would be needed to evaluate the change since the new devices can likely be assessed using nonclinical test methods. In the second example, if the new size would represent the new minimum or the new maximum of the implanted devices, clinical data may be needed to support substantial equivalence since the change in technological characteristic is expanding the range of device sizes.

The third scenario is when substantial equivalence cannot be determined by nonclinical testing, such as analytical, bench, or animal testing. In determining whether nonclinical testing is inadequate, such that clinical data may be needed, FDA recommends considering the following factors, if there is no model available, if there is an available model but that model is not adequate due to its limitations, if the model may not be predictive of clinical outcomes, or if there are anatomical and/or pathophysiological species-specific questions that rely on clinical evidence.

Here are a few examples. In the first example, substantial equivalence can't be determined by nonclinical testing for a device intended to treat schizophrenia due to the limited availability of nonclinical models for schizophrenia.

As another example, substantial equivalence can't be determined by nonclinical testing for an assay intended to screen blood donors for transfusion-transmitted infections because analytical testing cannot be used to adequately evaluate the clinical performance of the assay, or the risks associated with incorrect results.

As a third example, substantial equivalence cannot be determined by nonclinical testing for an in vitro diagnostic intended for point of care use when the predicate was not intended for point of care use. This is due to the variety of clinical environments and diverse populations that may use the device.

The fourth scenario is when a newly identified or increased risk for the predicate suggests clinical data may be needed for the new device. This may be the result of new scientific information becoming available based on experience with the use of the predicate. In request for clinical data due to a new or increased risk, we will provide an explanation of the reasons for the request and why it is necessary for a substantial equivalence determination.

Finally, I wanted to note that, as described in the Best Practices for Selecting a Predicate draft guidance, whenever possible, FDA recommends that manufacturers should not use certain devices as predicate devices if they exhibit new or increased risks, especially if an alternative predicate device exists without that new or increased risk.

On the left is an example where clinical data may not be needed. In this example, new information from recalls, adverse events, and literature has made FDA aware of malfunctions for a device. However, based on FDA's assessment, it's determined that nonclinical testing and labeling may adequately mitigate the risks, such that, clinical data may not be needed to demonstrate substantial equivalence.

On the right is an example where clinical data may be needed. In this example, new information suggests that there could be significant patient injury from the device in surgical procedures. In this example, the manufacturer ends up recalling the device and submitting a new 510(k) with clinical data to address the risk of significant patient injury. In this latter example, FDA ends up issuing a device-specific guidance with nonclinical and clinical testing recommendations for the device type.

In summary, this guidance clarifies and provides examples of situations when clinical data may be necessary to demonstrate substantial equivalence and is intended to help enhance the predictability, consistency, and transparency of the 510(k) Program. I will now turn it over to Dr. Yang, who will discuss the next guidance.

Peter Yang: Good afternoon. My name is Peter Yang and I'm the Program Lead for the De Novo Program, but I dabble in 510(k) occasionally, and I'm presenting this draft guidance, which we have titled Evidentiary Expectations for 510(k) Implant Devices.

Folks may not know this, but we review quite a few implants in the 510(k) space. This guidance is intended to provide a one-stop shop for our principles and recommendations for 510(k) implants. Of course, we then have device-specific guidances, which provide more relevant detail for those products.

We hope that, by putting everything into one place, that we can help industry walk through how they might think about their own implant. For example, we discuss human factors considerations for implants, including the implantation process, we discuss how collecting information on patient experience with a 510(k) implant can be used to help make the case for a device and support substantial equivalence decisions, and we provide recommendations for labeling, including the idea of implant cards to help patients be better informed and to help with their everyday living with an implant.

Just to be clear about what we're talking about here with respect to this guidance, an implant is actually defined by regulation, in this case, 21 CFR 860.3(d) as, quote, "a device which is placed into a surgically or naturally formed cavity of the human body, and that it is regarded as an implant only if it is intended to remain implanted continuously for a period of 30 days or more." So those are the kinds of implants that we cover in this guidance. However, we also thought about devices which are used for a period of time and then periodically replaced or refreshed, such that, while the exposure of any one device might be less than 30 days, there's, in fact, cumulative exposure over 30 days, maybe even life-long exposure. And so that kind of intended duration of exposure should factor into the thinking about testing.

So here are some of our general considerations, our guiding principles for 510(k) implants. And we broke it out into these three questions. The first question is, what are the indications for use? Obviously, testing should be tailored to the intended population, the disease state, and the location of implantation. That's true for any device, including when the device is indicated for pediatrics populations, and thinking about what data is appropriate to support use of the device in certain vulnerable populations, for example, in children.

The duration of implantation also matters. Some implants might only be implanted for about 30 days. Others are lifelong. It's possible to use shorter-term testing to extrapolate longer-term performance, but it's also important to test under worst-case implantation conditions. Especially for longer-term implants, those devices might experience increased wear and degradation. And so, this concept is really about tailoring evidence generation to the duration of implantation.

And then lastly, the patient and the physician experience with the implant is also important to consider. So typically, we might focus traditionally on the physician and their experience with implanting a particular device. However, it's also important to consider the patients' experience with the implant. Particularly for implants that are longer term, patients' everyday activities might be affected by the implant. It might affect how they travel or go through airport security. There might be maintenance or other kinds of obligations that patients need to know about to ensure that the implant continues to function as intended, maybe even software updates as well. These kinds of issues might factor into your risk analysis and your testing strategy for a given 510(k) implant.

So now we come to the recommendations part of the guidance. We have a number of categories of different kinds of testing that we discuss in the guidance. However, most of you will recognize some or all of these, things like biocompatibility, MR compatibility, corrosion and fatigue, degradation, imaging compatibility, et cetera. Most of these categories are cross-cutting issues that apply to all sorts of medical devices but, of course, apply especially to implants. For each category, we try to provide implant-relevant information. But we also link to the relevant cross-cutting guidances, which we go, which go into more detail on those specifics. And of course, we have a lot of cross-cutting guidances. For some issues, we have recommendations in a device-specific guidance on a particular topic, which could be relevant from a scientific perspective for other devices. To be clear, we're not saying that all of these

tests must be done for every implant. The testing is going to depend on the particulars of the device itself, including how it may be different from the predicate device.

As Mary just discussed with the previous draft guidance, clinical data might be needed. We may need information on the implant's design characteristics. For example, the raw materials, manufacturing, and processing steps can have a significant effect on the performance of the final finished form of a device. Examples include nitinol or ultra-high molecular weight polyethylene or devices using animal-derived materials.

I already mentioned human factors and usability testing, as well as collecting patient experience information and now I want to discuss labeling briefly. Of course, all 510(k) implants, like any medical device, should come with labeling, including basic elements like directions for use, its intended use, and so forth. But we encourage you to think more expansively about providing helpful information not only to the clinician implanting a particular device but also for patients. Sometimes patient labeling can be helpful to understand, to help patients understand their implant.

More specifically, we would suggest the concept of implant cards. Salient information about what the implant is, what it's made of, MR compatibility, as well as information for reporting any issues, in an easy-to-read form. We're not currently recommending any particular approach. Although, this general concept isn't new. The recently released MR labeling guidance discusses implant cards as well. Whichever approach you take, it's about empowering patients, so that they know what's inside their body and we think it's a helpful step for better patient safety. And that's it for this guidance on 510(k) implants.

These next two slides provide all references that are included in this slide deck. We've included the full URL for each reference, so that you can access them after the presentation.

As a reminder, the guidances that we have covered today are draft guidances and are not for implementation. You may comment on any guidance at any time. We're seeking your feedback on these draft guidances before the comment period closes on December 6th of this year, so that we can consider your comments on the draft guidances as we begin work on the final guidances. The draft guidances titles, docket numbers, and links to the dockets are included on this slide for your reference.

Before we transition to our question-and-answer time, I want to recap some important high-level points. The recommendations proposed in these new draft guidances are consistent with FDA's 510(k) Program guidance. We are not changing the applicable statutory regulatory standards, such as how FDA evaluates substantial equivalence or looks at other 510(k) requirements.

The new draft guidances we have written provide clarity on the 510(k) Program. I want to emphasize that we undertook this effort in direct response to public comments on the 510(k) Program. We do hope that these three guidances help to improve the transparency, predictability, and consistency of the 510(k) process by providing recommendations for these three topics, our recommended best practices for selecting a predicate device, providing some clarity and predictability for when clinical data may be necessary in a 510(k) submission, and a consolidation of our general recommendations for implants that are reviewed through 510(k).

On behalf of myself and the other presenters, thank you for attending today. And we look forward to taking some of your questions. I'll now turn it back over to Kim.

CDR Kim Piermatteo: Thank you, Peter. And thank you to Mary and Megha for your presentations today. We will now transition to our interactive question and answer segment of our webinar, where you get to ask your questions to our panel.

Joining our presenters today on our panel are Dr. Kathryn Drzewiecki, Policy Advisor in the Office of Policy in CDRH; Joshua Nipper, Director of the Division of Submission Support in the Office of Regulatory Programs within OPEQ in CDRH; and Angela DeMarco, Assistant Director of the 510(k), De Novo, 513(g), Device Determinations, and Custom Devices Life Cycle Team in the Division of Submission Support and the Office of Regulatory Programs in OPEQ as well. Thank you all for joining our panel.

Before we begin, I'd like to go over how we will manage the segment and a few reminders. 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, 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. We appreciate that you may have a very specific question involving your device or scenario. However, we might not be able to address or answer such specific questions. Therefore, we'll try to frame a broader response based on what's proposed in the guidance documents.

And our panel today is available to you to help you better understand and get clarity on what we intend in these draft guidances. So we ask you to try to frame your question with this in mind. After you ask your question, please lower your hand and if you have another question, please raise your hand again to get back into the queue and I will call on you as time permits.

Now, as we wait to receive your questions, I'd like to welcome our newest panelists with some questions we have gotten over the past few weeks about these guidances. For our first question, I'd like to ask Kathryn if she could start us off by providing additional information on how to comment on draft guidances. Kathryn.

Kathryn Drzewiecki: Thanks, Kim. And I think this is a nice follow on to Peter's note about draft guidances since the guidances we discussed today are draft. And so just a reminder and a refresher for some, new information for others that you can comment on any guidance at any time. The dockets for guidance documents remain open, but your comments may not be acted upon by us until the document is next revised or updated. So, for these three draft guidances, we highly recommend that you submit any comments you may have by December 6th to their respective dockets, so that we can, in fact, consider your comments while we work to finalize these draft guidances.

CDR Kim Piermatteo: Great. Thanks, Kathryn. Now for our next question, I'll be directing that to Josh. Josh, the question is, why is FDA issuing these new draft guidances on the 510(k) Program now?

Joshua Nipper: Thanks, Kim. And I'd also like to reiterate my thanks to the three presenters earlier. As you heard about in today's presentation, CDRH is issuing these three draft guidances in response to our request for comments on the 510(k) Program. In particular, a proposal to post on our website those

clear devices that demonstrated substantial equivalence to predicate devices that were greater than 10 years old, as well as other feedback that could help improve the 510(k) Program.

More broadly, CDRH believes in the merits of the 510(k) Program and has continued to make improvements to our largest premarket program over the past decade to assure it continues to meet the needs of patients, provides appropriate patient safeguards, and supports decision making that is based on sound science. We intend for these three draft guidances, when finalized, to enhance the existing 510(k) Program by providing clarity on complex device topics and 510(k) submissions, which we hope to help optimize the predictability and consistency of the 510(k) Program as well as help CDRH implement our MDUFA V goals.

CDR Kim Piermatteo: Thanks, Josh. Alright, our next question, I'll be coming to Angela. Angela, the question is, what has FDA done to ensure that information about 510(k) devices is easily accessible to industry, patients, and other interested stakeholders?

Angela DeMarco: Thanks, Kim. Great question. So, FDA identifies all devices cleared through the 510(k) process in the publicly available FDA 510(k) database and that is updated monthly. Nearly all modern, legally marketed devices also have publicly available 510(k) summaries, indications for use documents, and substantial equivalence letters. We also have our total product life cycles database, which integrates premarket and postmarket data about medical devices. These databases provide information for all stakeholders, including the basic administrative information that industry can use to begin identifying valid predicate devices and information about the device and its intended use that patients or health care professionals may wish to know.

CDR Kim Piermatteo: Thanks, Angela. And thanks, Josh, again, and Kathryn. So we'll now take our first live question. Our first live question is coming from J. Mayhall. I have unmuted your line. Please unmute yourself and ask your question.

J. Mayhall: I'm sorry. I think I raised my hand by accident.

CDR Kim Piermatteo: OK.

J. Mayhall: Apologies.

CDR Kim Piermatteo: No worries. That's OK. Thank you. We'll move down to our next hand. Our next caller is Jang. Jang, I've unmuted your line. Please unmute yourself and ask your question.

Jang, are you able to unmute your line?

Alright, we will move down to the next stakeholder. Rama. Rama, I've unmuted your line. Please unmute yourself and ask your question.

Rama, are you able to unmute?

Alright, hearing none, we're going to move down to Stephanie. Stephanie, I've unmuted your line. Please unmute yourself and ask your question.

Stephanie, are you able to unmute?

Alright, I am hoping that I'm going to get someone. The next person that I'm going to call on is Cyrina Swanston. I've unmuted your line. Please unmute yourself and ask your question.

Cyrina Swanston: Hello. Can you hear me?

CDR Kim Piermatteo: Yes. Thank you. Thank you, Cyrina.

Cyrina Swanston: Hi my name is Cyrina, and I had a question regarding the recommendations for use of clinical data in 510(k)s, specifically regarding the timeline. So, say we picked a predicate device and have started collecting clinical data, but then our predicate device is found to be recalled due to a design-related issue. This is just theoretical. What is FDA's thinking in that situation? How would the manufacturer have to handle that?

CDR Kim Piermatteo: Thank you for that question. Mary, did you want to provide a response first, or anyone else on the team?

Mary Wen: Yes, I'm happy to. And thank you for that question. That is a great question. If you have already started collecting clinical data and you notice that there is a recall or an issue with the predicate device, we encourage you to reach out to FDA right away to begin having those types of conversations about whether there is a difference in the level of evidence needed.

In this case, though, it sounds like, you know, the company has already started collecting clinical data. And the question has to, or the recommendation and the guidance has to do with generally when clinical data is not needed and a new risk or an increased risk results in the need for clinical data. So, I just wanted to be clear on that, that, you know, this company is already collecting clinical data and so that may not mean that there may be an increased level of evidence needed.

Cyrina Swanston: OK. Thank you very much.

Mary Wen: Thank you.

CDR Kim Piermatteo: Yes. Thanks, Mary, for that response. Alright, our next question is coming from Lucy. Oops. Sorry. Vivek. Vivek, I've unmuted your line. Please unmute yourself and ask your question.

Vivek Raut: Hello. Can you hear me?

CDR Kim Piermatteo: Yes, we can.

Vivek Raut: Very good. So this is more of a technical question. I heard that these are draft guidances and still not finalized. We are in the middle of putting together a 510(k) submission package. Do we have to adhere to these new recommendations, especially on providing a justification for a valid predicate device, given that the predicate device may be older, more than 10 years old? What is the expectation with the upcoming submissions while these new guidances are in the draft format?

CDR Kim Piermatteo: Thank you, Vivek, for that question. I'd like to turn it over to Kathryn, or Megha if you want to chime in as well, but, Kathryn, would you like to start?

Kathryn Drzewiecki : Sure, Vivek. I'll just chime in and say that these draft guidances are not for implementation at this time. So the recommendations and the guidances are they're draft. You can proceed with the 510, with your 510(k) submission consistent with the current finalized guidance that's available. And in terms of when the guidances would be finalized and the implementation timeline, we would cover that when the guidances will be finalized and when it would be time to implement them. Megha, did you have anything to add?

Megha Reddy: Nope. Nothing to add. Thank you, Kathryn. The only thing, I guess, I would add is, as Kathryn said, the finalized guidances, the 510(k) Program guidance would be primarily what you'd use in addition to any other device-specific guidances that you have, that are finalized.

Vivek Raut: Understood. Very good. Thank you.

CDR Kim Piermatteo: Thanks, Kathryn and Megha. And thanks, Vivek, for that question. Alright, now I'm going to come back. Lucy. Lucy, I have unmuted your line. Please unmute yourself and ask your question.

Lucy, are you able to unmute your line?

Alright, I'm going to go to Allison. Allison, I have unmuted your line. Please unmute yourself and ask your question.

Allison Komiyama: Alright, can you hear me?

CDR Kim Piermatteo: Yes, we can.

Allison Komiyama: Alright. Yay. So great presentation. Super excited about these draft guidance documents. One question I had was about the clinical guidance. One of the areas where I have seen 100% clinical data necessary in order to get clearance is with our class I devices that exceed the limitations of the exemption. And I know the guidance makes very brief mention of it and adds that very small sliver of submissions in the footnote.

But what my question is is, oftentimes, when we submit these 510(k)s with fairly substantial clinical data, I think because there's not a lot of, or typically, there's not much review of these files, right? Typically, they're class I or even for the class II 510(k) exempt devices that we end up having to submit a 510(k) for, they just get bogged down in the requirements for the clinical testing, even though FDA has already decided that they are low risk or even class II 510(k) exempt.

So question is, does FDA have any recommendations? Or will you be adding, hopefully, to the guidance on what sort of benefit-risk considerations? What should we add to the file to help reduce burden on the clinical evidence that is needed for these clearances?

CDR Kim Piermatteo: Thank you, Allison. I'm going to turn it over to Mary.

Mary, did you want to provide a response?

Mary, are you able to unmute?

Mary Wen: Yes. Sorry about that. Thank you, Allison, for that comment. And great to hear your perspective on your experience with class I devices.

First of all, I just wanted to say that this is a draft guidance and not for implementation. And so we would love to invite you to comment to the docket if you have a suggestion on how you would like to see the guidance revised. You know, we'd love to hear more about your experience with class I devices that tripped the limitations and your experience with providing clinical data for that. And we'll consider it and see what recommendations we can put in the guidance. Thank you.

Allison Komiyama: Awesome. Thank you.

CDR Kim Piermatteo: Thanks, Mary.

Joshua Nipper: This is Josh. Just wanted to add. I think when you're dealing with, especially class I or class II exempt, that we don't see often, but there is something let's just say new or novel that is tripping the limitations. I think it would be good to come in and have that conversation. Certainly, in the Pre-Submission Program is a good pathway for having those questions floated out ahead of time. So that, we aren't unnecessarily getting bogged down with looking at clinical data or getting too into the weeds for something that might be a relatively low risk. But certainly, if that clinical data is needed to get a clearance, then I think we have to do a full review of that data, regardless of the exact regulatory classification. So come to us early. Float the questions out. And hopefully the benefit-risk aspects of the 510(k) can be discussed before the submission comes in. So that, hopefully, we're as on the same page as we can be.

CDR Kim Piermatteo: Thanks, Josh, for that additional comments. Alright, the next person I'm going to call on is Mary. Mary, I have unmuted your line. Please unmute yourself and ask your question.

Mary Mellows: Thank you so much. My question has been asked kind of already, but what I'm curious about, if I'm in the midst of drafting a submission for an implant that doesn't currently have an implant card, what is the best guesstimate in terms of when we're thinking these draft guidances will be formally implemented? Do we have a best guess yet?

CDR Kim Piermatteo: Thanks, Mary. I'll open it up to anyone on the team who wants to provide a response regarding timing of the webinar, or sorry, timing of the guidance, when they'll be finalized.

Kathryn Drzewiecki: Yeah. So I can start. This is Kathryn. Mary, in terms of guidance development, it's a lengthy process on our end. We comply with good guidance practices in accordance with 21 CFR 10.115 and after the comment period closes on December 6th, we consider all comments received. And we prepare a final version of the guidance that incorporates any suggested changes that we can. And the guidance goes through review and clearance. And once it's published, we'll publish a federal register notice announcing the final guidance is available. And that process can really depend on how many comments are submitted and the available resources to work on those guidances.

In terms of also implementation, that's something we'd be interested in feedback on in terms of if the guidance is finalized and you're working on a submission. And so that's definitely something that you can provide comment on to the docket as well. I don't know if anyone else from the team wants to chime in, but hopefully, that was a helpful overview of what we have left to help, what steps we have left that will need to be taken care of to finalize these documents.

Peter Yang: This is Peter Yang. I just wanted to add on. If you read through the draft guidance itself and you look at our recommendations around implant cards, there's no specific format or system that we're sort of advocating for in terms of what it should look like or the exact data that should be included on that card. And so, there's a fair amount of flexibility here. We're trying to enter into a space where we're trying to empower patients and provide more information. And so certainly your feedback on what you think would be appropriate to include in an implant card, questions about formatting, maybe there are things that we can address there.

But certainly, we want to it's not so specific to where we would, say, mandate, especially since this is guidance or recommendations, that we would mandate any specific content be in there. So I think what we're, from my perspective, I think we're looking forward to working with you in the actual submission eventually whenever this guidance gets finalized with that information. We're working we're interested in working with you on what a best practice would be.

And as we get more experience with that, we might be able to refine the guidance to provide more information. And certainly, we can refine the guidance according to your feedback as well. So, any thoughts that you have, we'd love to hear them.

CDR Kim Piermatteo: Thanks, Peter and Kathryn. Thanks, Mary, for your question. Our next question is coming from Shikha Malik. I've unmuted your line. Please unmute yourself and ask your question.

Shikha Malik: Hi. Good afternoon. So, my question is, is there any change in the FDA expectation for like documentation requirement based on the new draft guidance document?

CDR Kim Piermatteo: Are you talking-- can you clarify your question? Are you talking specifically about one of the three or just the documentation in general?

Shikha Malik: In general.

CDR Kim Piermatteo: OK. Josh, did you want to provide a response?

Joshua Nipper: Yeah. I mean, I think, as we said earlier, these are draft guidance documents, so not for implementation. None of the three guidances that we discussed today are things that you need to be addressing in the 510(k) that you submit tomorrow. I mean, they do provide some good best practices and so, we definitely recommend looking through them and understanding what they say.

But at this point, the best recommendation is to look at the ESTAR template online, walk through that, follow any cross-cutting biocompatibility or device-specific guidances that exist. But if you're submitting an implant tomorrow, there is no need to cite the draft implant guidance. There's no need to discuss how you have met the individual criteria until that device were to go final. And you know, we've gotten questions on the timing and the implementation of that. And that's all things that we will work out as

the guidances as we receive your comments to the docket and can look at the feedback that we get from our stakeholders.

CDR Kim Piermatteo: Thanks, Josh. Alright, our next question is coming from Tosan. Tosan, I've unmuted your line. Please unmute yourself and ask your question.

Tosan Eweka: Hi. Can you hear me?

CDR Kim Piermatteo: Yes, we can.

Tosan Eweka: So, my question is with respect to the 510(k) summaries. Specifically, is the FDA taking any steps to ensure that the information disclosed in the 510(k) summaries are consistent across the different review branches? And I ask this because there are times that some 510(k) summaries will list specific tests in a predicate device conducted. And then some other 510(k) summaries don't have any information. And there are no guidance documents that you can go to to determine what testing is applicable.

CDR Kim Piermatteo: Thanks, Tosan, for your question. I'll turn it over to Josh to provide a response.

Joshua Nipper: Yeah. Sure. It's a fantastic question. And it is something that we are actively looking at. This webinar is focused on the three draft guidances that we've published. There are other attempts at the 510(k) modernization that we are consistently working on. 510(k) summaries is something we're looking at. It is, we recognize that there is inconsistency across the eight office of health technologies.

We get roughly 3,500 to 4,000 510(k)s a year. So ensuring consistency across that many, it's a difficult task. We're continuing to look at ways to further that consistency, both within the required ESTAR template now and other things internally. Certainly, if you have ideas or suggestions, we're open to that feedback. But, you know, it is a challenge. And we recognize that it's a challenge. But we are continuing to try to move that forward, so that we're at least getting some base level of consistency across the types of things that are being reported in there.

CDR Kim Piermatteo: Thank you, Josh. Alright, our next question is coming from Kristin. Kristin, I've unmuted your line. Please unmute yourself and ask your question.

Kristin Duggan: Hi. Thank you. Kristin Duggan at Hogan Lovells. I had a question about the predicate selection guidance. So, I guess I wanted to understand more about your thoughts, about how FDA will handle it when a company selects a predicate that's a valid predicate but not, that wasn't chosen using the best practices. So, either, there was no predicate that follows the best practices, or perhaps, they selected another one because it was closer to their device. If there's some sort of issue with the predicate or how they tested, it doesn't necessarily mean the new device is not substantially equivalent, which is, obviously, the standard. And I can see potentially situations where you're sort of asking a new company to deal with issues from a prior device, essentially. So, I just wanted to hear your thoughts on that.

CDR Kim Piermatteo: Thanks, Kristin, for that question. I'm going to turn it over to Megha to provide you a response.

Megha Reddy: Thanks, Kim. Great question, Kristin. You know, like I mentioned, we mentioned here, the guidances are recommendations. They provide recommendations for best practices. So, they're really meant to help be a guide to use to select the best predicate, the best valid predicate for the subject device. So, if one is unavailable or there's a different reason why a different predicate is selected, in the guidance, we did have a little have an example of that in there, where we recommend that you include a description within the main 510(k) submission of why you selected that predicate. So, you know, it gives the sponsors an opportunity to share that background and that knowledge with the FDA reviewers that can be taken into consideration.

CDR Kim Piermatteo: Thanks, Megha. Our next question is coming from Kristie. Kristie, I have unmuted your line. Please unmute yourself and ask your question.

Kristie Diep: Hi. Thank you. This is another question related to the implant cards. And the concept of implant cards, of course, is not new to medical device manufacturers. This has been out there for a number of years now under EU MDR.

We note that the draft guidance, in its current form, does not appear to consider any of the exceptions that are clearly noted in MDR for things like, say, a suture, which isn't really going to need maintenance and updates and that the patient does not interact with, and, frankly, is going to finish its role right within weeks or just a few months. Can anyone on this group comment on why FDA did not align their thinking with EU MDR on that topic?

CDR Kim Piermatteo: Thank you, Kristie, for that question. I think I'm going to turn it over to Peter or Kathryn if you want to provide a response.

Peter Yang: This is Peter Yang. Thanks for the question. I think harmonization is always something that we're thinking about. And certainly, sutures exist in the United States. And so, I think something like implant cards might make less sense in those cases, right? And so, this is not a requirement, you know, that we would plan to enforce on every implant device. These are things that could be helpful to empower patients living with an implant. So, you can think about the kinds of devices for which this information might be more important than others.

Maybe there is a time where a suture, because of its particular technology, may benefit from having an implant card. But it would-- I think it would be a device-specific consideration. And so certainly, if you have feedback in terms of how we could better harmonize with other agencies, so that it's consistent for industry and that what you do in one jurisdiction will work well in another, we'd certainly welcome that. To be clear, we are focused on the U.S. We're the U.S. FDA. And so we're focused on the United States market. But certainly, where we can harmonize, we should. And so welcome your feedback if you want to refine how we approach these considerations and provide some further improvements. We're very happy to consider those. Thank you.

CDR Kim Piermatteo: Thanks, Peter. Thanks, Kristie, for your question again. The next question is coming from Max. Max, I have unmuted your line. Please unmute yourself and ask your question.

Max Alfonso: Hello. Can you hear me?

CDR Kim Piermatteo: Yes, we can.

Max Alfonso: Awesome. My question is related to the best practices for selecting a predicate device. You mentioned the MedSun as well as the MAUDE databases to review for adverse events. I was wondering if you could explain a little bit about the differences between the MedSun database and the MAUDE database. Should we be looking for specific pieces of information in each database? Or should we just kind of do a general review? Just any sort of information would be great.

CDR Kim Piermatteo: Thanks, Max, for your question.

Megha Reddy: So, I can take a stab at this first. And, Josh, Angela, if you have anything to add, please feel free to jump in. In general, we listed those in the guidance. Really, it is like a general search. You want to review overall to make sure that there is no spike in adverse events or anything concerning that that's in there. So yeah, generally to look at. There's nothing specific that I would call to.

Joshua Nipper: Yeah. And this is Josh. I would add they're meant to be examples. Sometimes the different data sources have different green flags or red flags, if you will, in them. It's not an all-inclusive list. Certainly, if you're aware of published literature or an EU resource where the identical device is available somewhere else and it's been recalled and causing significant adverse events, that would be a situation where it's probably not the ideal predicate.

And so, looking at that and doing a comprehensive assessment of what you're picking as your predicate and how you may have different safety improvements, different adverse event risk profiles, that kind of thing is really the gist of what we're trying to say in the guidance. And so rather than focus on one database or one source of information, it's really getting a general sense of how the predicate device is performing and what that's looking like in real clinical practice.

CDR Kim Piermatteo: Thanks, Megha. Thanks, Josh. And thank you, Max, for your question. Our next question is coming from Nicholas. Nicholas, I've unmuted your line. Please unmute yourself and ask your question.

Nicholas Bergfeld: Yeah. Hi. Thanks so much for taking this question. I'm a researcher out of Texas Tech University. I had a question going on databases. So a lot of this for predicate is based on the idea of having information, whether that be the 510(k) Summary or the 510(k) filing in the FDA's searchable public database. Oftentimes, as you go farther back in these filings, less and less of them are uploaded. And so, I'm just curious, what alternative means exist to pull these documents for the utilization of a predicate?

CDR Kim Piermatteo: Thanks, Nicholas, for that question. Did anyone on the team want to chime in? I know this is a more general one regarding Freedom of Information.

Joshua Nipper: Well, I can take a stab. You know, I think that our summaries at least go back quite a ways. And if you recall, going back, we started this journey with questioning whether there was a time window. We, I think throughout 10 years or something like that, that the best predicate should be considered under because it's using more modern reviews, more modern disclosure on our 510(k) summaries, that type of thing. We heard pretty significantly from our stakeholders that it wasn't based on a time window, that it was based on a multitude of factors, which we've tried to encapsulate in this guidance. I think when you go back a ways, the information is there. Certainly, going back further than

that, if there is something that we've cleared, let's say in 1990, that is not online, realistically, the Freedom of Information Act is probably the most efficient way to get that information.

But it's a struggle to balance the sort of newness of getting a new and modern predicate versus something that's been around for a long time and works really well. But certainly, if there is something that, you know, is not, appears that it should be posted and it's not, you can reach out to the program staff and you know, you can ask the question, is this a database issue or error? And sometimes it is. There are times when there are something just glitches and it doesn't get posted right, in which case, we can sometimes get that put online.

CDR Kim Piermatteo: Great. Thanks, Josh. Thanks, Nicholas, for your question. Our next question is coming from Leslie. Leslie, I've unmuted your line. Please unmute yourself and ask your question.

Leslie: Hello. Can you hear me?

CDR Kim Piermatteo: Yes, we can.

Leslie: Great. Thanks for the presentation. I have a question related to predicate selection for an IVD. So when selecting a predicate from the valid predicate options, there are sometimes technical considerations that are also important. An example could be measuring interval. So where do the technical considerations fit within the best practices for choosing a predicate?

CDR Kim Piermatteo: Thank you, Leslie, for that question. Megha, did you want to start with a response? I know this is specifically related to an IVD predicate.

Megha Reddy: Yeah. So, in general, you would still follow the 510(k) Program guidance in terms of how you would select the predicate. The best practices and predicate guidance is really meant to be in addition to that and to be used in conjunction with it. So, you would definitely still take into account your technical considerations as you would normally when selecting a predicate device.

CDR Kim Piermatteo: Thanks, Megha. Our next question is coming from Grant. Grant, I've unmuted your line. Please unmute yourself and ask your question.

Grant: Yeah. My question is also related to the clinical testing requirements. If we select a predicate that has clinical testing as part of their 510(k) submission, would we also need to conduct similar clinical testing as part of our submission to establish substantial equivalence? Or are the cases where nonclinical testing would still be sufficient for that?

CDR Kim Piermatteo: Thank you, Grant, for that question. I'm going to turn it over to Mary to provide a response.

Mary Wen: Yeah. Great question, Grant. And the answer is not necessarily. Generally, if the intended use and technological characteristics of a new device are the same or at or sufficiently similar to that of the predicate, a new device that is subject to 510(k) requirements may be able to demonstrate substantial equivalence through robust nonclinical safety and performance data. However, in some cases, clinical data are necessary. This draft guidance, when finalized, provides certain scenarios when clinical data may be necessary and so we suggest that you still go through the guidance, consider the

factors. And if you have specific questions about a specific situation, we recommend that you reach out to the appropriate review division by submitting a pre-submission. Thanks.

CDR Kim Piermatteo: Thanks, Mary. Alright, our next question is coming from Hannah. Hannah, I have unmuted your line. Please unmute yourself and ask your question.

Hannah Matthews: Hello. Thanks, Kim. And thank for all for the presentation on those draft guidances. I have a question around the predicate selection. So in some cases, there's no suitable predicate under the right product, FDA product code. But the intended use for another device is identical. And sometimes that's because it's a historical predicate that's gone under a different product code in lieu of the correct one. Do you have any guidance around how to manage that?

CDR Kim Piermatteo: Thank you, Hannah, for that question. Angela, did you want to take a first response? Or someone else can join in from the team?

Peter Yang: This is Peter Yang. Let me jump in here. So, one of the things that we've tried to work through with especially with the 510(k) Program guidance, and because you're, the way that you've asked your question suggests, I mean, sometimes there's combinations of intended use and technology that remain within a given regulation. And so it could be suitable to submit a 510(k) under that scenario. What we have tried to move away from, especially in our 2014 program guidance, is the use of split predicates. Where you adopt the intended use or the indications for use from one device, but you adopt the technology from a device in a completely different regulation.

And so, where that combination may be the case, we would generally recommend that you come to us with a Pre-Submission. Because in that case, it's possible that your device may or not make it through the 510(k) flowchart, that at decision point two or point four of the flowchart, which you can look at in the program guidance, that it may fall off the flowchart in that way. It depends on the specifics of the exact changes that you're making to the indications for use in technology. And so generally speaking, it helps to talk with the review division and their experience with those kinds of devices and technologies to understand how your device might fare out. And so generally, maybe you email the assistant director that's sort of in charge of those kinds of products and maybe ask the question or a Pre-Submission, or a 513(g) request for information submission would be the appropriate way to work through some of those questions.

Hannah Matthews: Great. Thanks, Peter.

CDR Kim Piermatteo: Great. Thanks, Hannah, for the question. Thanks, Peter, for the response. Our next question is coming from Sudeep. Sudeep, I've unmuted your line. Please unmute yourself and ask your question.

Sudeep, are you able to unmute your line?

Alright, our next question is coming from Steve. Steve, I have unmuted your line. Please unmute yourself and ask your question.

Steve: Yes. Hello. Are you able to hear me?

CDR Kim Piermatteo: Yes, we can.

Steve: Thank you very much for this time. My question, I guess, is a little bit of a two part. So my name is Steve. I'm a consultant with Spearhead.

The first part is let's say a manufacturer has a list of multiple potential predicates. But none of them actually fully meet the guidance requirements. So, they're going to have the, they're going to pick whichever they think is the best fit. Maybe some have recalls, some have technological differences or other variations in intended use. My first part, I guess, is, do you expect a rationale not just for the selection of the predicate but also for the exclusions of other ones which could have been predicates but were excluded?

And the second part is, do you foresee maybe a scenario where a manufacturer selects a predicate from a list of a number of predicates which may not all be perfect where there would be maybe differences in the opinion between what the reviewer thinks would be the appropriate predicate and what the manufacturer thinks and how that would be addressed? Thank you.

CDR Kim Piermatteo: Thanks, Steve, for that question. Megha, would you like to provide a response?

Megha Reddy: Sure. Thanks, Steve. That's a great question. I, in general, you know, yes, there are multiple predicates that you could select. And the sponsor will pick the best one that they think fits. In the guidance, we do have an example of a chart that lists out the top few predicates that there are and what the issues are. And we recommend including something of the sort. And so that would help us better understand why the one predicate that was chosen was chosen.

And so it kind of shows how each of the top, let's say, four predicates that you've selected, which best practices fit into which ones. And then you could include a short rationale for why you selected the one that you selected. And this would, of course, be in the submission. The summary can have a shorter version of that.

CDR Kim Piermatteo: Thanks, Megha. Thanks, Steve, for your question. Our next question is coming from Stephanie. Stephanie, I've unmuted your line. Please unmute yourself and ask your question.

Stephanie Wilde: Hi. Can you hear me?

CDR Kim Piermatteo: Yes, we can.

Stephanie Wilde: Oh, great. So can you comment on the frequency for which the FDA is seeing 510(k) submissions that are requiring clinical data to determine substantial equivalence? And is that trending, that frequency trending upwards?

CDR Kim Piermatteo: Thanks, Stephanie, for that question. Mary, did you want to provide a response? Or Josh, I believe.

Joshua Nipper: I can take a rough estimate on, this is Josh. It's around 10%. You know, it is a not always an easy question to answer. I don't think we've seen any significant trends going one direction or the other. We have constant fluctuations in our 510(k)s being submitted both due to new and novel

technologies. And certainly, the pandemic has shifted the types of submissions we were seeing for a while there. So, you know, obviously, like PPE was pretty consistent not including clinical data. So it's a best estimate. It's usually around 10% of 510(k)s. That's the closest we'd have to a official answer.

CDR Kim Piermatteo: Thanks, Josh. Thanks, Stephanie, for your question. Our next question is coming from Ali. Ali, I've unmuted your line. Please unmute yourself and ask your question.

Ali AbuSaleh: Hey, there. Can you hear me?

CDR Kim Piermatteo: Yes, I can.

Ali AbuSaleh: Sounds great. We just, it's kind of a two parter here, but we received some guidance from a reviewer more recently and it looks like the agency's trying to avoid having secondary, too many reference devices. I just wanted to confirm that.

And then when it comes to the draft guidance and what we put into the 510(k) summary, would we include just the primary predicate and a summary of why we chose that? Or would it be the full gamut of primary, secondary, and reference device? Thanks.

CDR Kim Piermatteo: Thanks, Ali, for your question. Since this is surrounding predicates in general, Angela, did you want to provide a response? Or, Megha?

Angela DeMarco: Yeah. This is Angela. I can jump in for the first part of that and then if Megha has anything to add on, she can. But as for whether or not you should include additional information into the 510(k) Summary, we do recommend that anything that is the basis of the substantial equivalence decision to be in the 510(k) Summary. So, if you did identify a secondary predicate as the basis of your substantial equivalence decision, we do recommend that you provide a summary of that predicate in your 510(k) Summary.

Megha Reddy: Thanks, Angela. And just to jump in as far as the best practices go, we would want, we would expect to see a rationale for the predicates that you did end up selecting, if it happens to be more than one.

CDR Kim Piermatteo: Great. Thanks, Angela. And thanks, Megha. Thanks, Ali, for your question. Our next question is coming from Geeta. Geeta, I've unmuted your line. Please unmute yourself and ask your question.

Geeta Pamidimukkala: Hi there. Thank you for taking my question. So, the predicates draft guidance in particular seems to be aimed at device manufacturers to use while they're preparing the 510(k) submission. But the guidance doesn't discuss how or to what extent the guidance will be implemented by the FDA review staff during the course of the review. So, for example, if the selected predicate didn't follow the recommendations in the guidance, how could that affect the review with respect to the deficiencies issued?

CDR Kim Piermatteo: Thanks, Geeta, for that question. I'm going to open it up to the team. Is there someone who wants to provide a first response?

Megha Reddy: I can take the first stab at that question. Thank you for the question, Geeta. I would, that's a great point that you've made, and it is something that would be helpful in the guidance. I would recommend that you include that as part of the comments in the public docket and it's something that we can definitely take into consideration during our review.

CDR Kim Piermatteo: Thanks, Megha. Thanks, Geeta. Our next question is coming from Rama. Rama, I've unmuted your line. Please unmute yourself and ask your question.

Rama, are you able to unmute?

Rama: Yeah. Can you hear me?

CDR Kim Piermatteo: Yes, I can.

Rama: OK. So, this is a bit of a two-part question, but it's related to the same device. I mean, so what I mean by that is you have a device that is for, what do you say, on site or point of care. And then you want to take it to home. So, you probably have to do some clinical, provide clinical data is what you may get as a recommendation from your Pre-Sub, Q-Sub meetings. And then when you take it home, the whole user environment is very different. And the variance that can come from is a lot more. And I would anticipate that the request for additional clinical data will come, as this is a very general category of devices mentioned. So, I just want to hear something about this.

CDR Kim Piermatteo: Thanks, Rama. Can you clarify just quickly what your question is for us, please?

Rama: Sure. So during COVID, we saw that, a lot of times, things, point of care, IVDs, you could go to a hospital or some other clinical health center and get that done. But during COVID, a lot of people were sent home and given some devices to collect the data to monitor them remotely. And this is becoming a trend even after the COVID, right? So, in such cases to get the predicates and maybe you say I'm a new manufacturer and have picked the predicate of a device that is already used at point of care and now I want to take this same device to home for home use or outside of point of care use. And what would be the clinical data requirements in the second case, assuming that I got the 510(k) from the predicate device of point of care along those lines?

CDR Kim Piermatteo: OK. Thank you. Thank you for clarifying. Yeah. I think you're talking about the environment of use, correct? Changing it?

Rama: Yeah. Yeah.

Joshua Nipper: Yeah. This is Josh. that's a great question. And it's certainly something that we struggle with a little bit. FDA does not regulate practice of medicine. And so, if a device is indicated for, let's just say, in-clinic use and clinician decides sending that home is in the best interests of the patient, totally OK.

For devices indicating for home use or point of care use, et cetera, that needs clinical, we do our best to get the best information we can, be that a clinical study, be that human factors testing. So, if a device is indicated for the lay user at home and that's in its indications for use and its labeling, we do a human factors assessment or we expect the companies to do the human factors assessment, to ensure that can

be used safely and effectively in the environment indicated. Certainly, COVID put a challenge on the global health care. And we had to adapt quickly, as did our regulated industries and patients and clinicians. But at the high level, I would say, if a device is being indicated for home use, we would at least want to see some testing, be it clinical or human factors, to validate that it's safe and effective for its intended use. Anyone else want to jump in there and things that they've seen?

Peter Yang: Yeah. This is Peter Yang. So, it actually helps that I have some experience with some of the recent COVID de novos that have been granted. And so, there are, we have one regulation which we created for point of care COVID tests. And we have one regulation that we created for OTC COVID tests. And so, you're welcome to take a look at those. The granting orders are public on our website. But the question of changing the user environment, changing where the test is administered, does that change in environment represent a change in intended use? Or does it raise new risks when you're transitioning from point of care to home? And I think some people would argue yes. But certainly, it can depend on the particular test, the complexity of collecting a sample and so forth.

And so, for COVID tests, we differentiated between the two based on the different environments. And so, there's going to be different testing for when you're doing something over the counter or collecting at home. There might be flex studies that you might need to do. There's other kinds of considerations. And so, I'm not an expert in IVDs. What I would suggest is for your particular application to reach out to the Office of Health Technology Seven, who reviews in-vitro diagnostic devices, and run your question by them in the form of pre-submission and get their take on what kinds of data requirements might be necessary and what the next steps would be for your particular device.

Rama: Thank you.

CDR Kim Piermatteo: Thank you, Rama. And thank you, Josh and Peter, for your comments.

Rama: I have a question still, additional question. In the sense that this is OTC is what Peter mentioned, but it's very likely that it may not be OTC. And it could be prescription. I just wanted to mention that.

CDR Kim Piermatteo: OK.

Peter Yang: This is Peter Yang. Thanks for that. And again, it just depends on the specifics of the particular device and the risks involved.

Rama: Right. Thank you.

CDR Kim Piermatteo: OK. Thank you, everyone. With that, that wraps up this webinar's question and answer segment. So thank you everyone for your active and engaging participation. We appreciate it. I'd like to turn it back over to Josh right now for his final thoughts on today's topic. Josh.

Joshua Nipper: Yeah. Thank you, Kim. And want to reiterate again, thank you to all the presenters and panelists. And we didn't say it today, but there is a ton of work in getting these draft guidances out there and so, for anyone listening in, thank you for all the help.

I want to just thank everyone for joining today to hear about our recent efforts to improve transparency, consistency, in our largest premarket program, that is the 510(k) Program. These guidances, when

finalized, can help address the increasing complexity of and advance the safety and effectiveness of medical devices. But we do want to hear from you. So please submit your comments on these draft guidances to their respective dockets by December 6th, so that we can consider them in finalizing the guidances.

And with that, I'd like to wish everyone a good afternoon. Thank you.

CDR Kim Piermatteo: Thank you Josh for those final remarks. And thanks again to all of our presenters and panelists for today. For your information, printable slides of today's presentation are currently available on CDRH Learn at the link provided on this slide under the section titled, How to Study and Market Your Device and the subsection, Premarket Notification (510(k)).

A recording of today's webinar and a transcript will be posted to CDRH Learn under this same section and subsection in the next few weeks. A screenshot of where you can find these webinar materials has been provided on this slide.

If you have additional questions about today's webinar, feel free to reach out to us and DICE at DICE@fda.hhs.gov

And lastly, we hope you're able to join us for a future CDRH webinar. You can find a listing of our upcoming webinars via the bottom link on this slide at www.fda.gov/cdrhwebinar.

Thank you all again for joining us. This concludes today's webinar. Take care.

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