Breakthrough Devices Program Updated Final Guidance
November 14, 2023

Moderator: CDR Kim Piermatteo

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

Our topic today is the final guidance titled "Breakthrough Devices Program," issued on September 15, 2023. The Breakthrough Devices Program is a voluntary program for certain medical devices and device-led combination products that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. The program is intended to provide patients and health care providers with timely access to medical devices by speeding up development, assessment, and review for Premarket Approval, 510(k) clearance, and De Novo marketing authorization.

During today's webinar, we will discuss the updates made to the final guidance, share how the program can help advance health equity, and answer your questions about the updated final guidance.

Before we begin, I'd like to provide two quick reminders for the webinar. First, please make sure you've joined us through the Zoom app and not through a web browser to avoid any 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 the FDA's Office of Media Affairs at FDAOMA@fda.hhs.gov.

I now have the pleasure of introducing our presenter for today's webinar. Ouided Rouabhi, Assistant Director of the Policy and Operations Team One within the Division of Clinical Evidence and Analysis in the Office of Product Evaluation and Quality, or OPEQ, in CDRH. We'll begin with a presentation from Ouided, and then field your questions about the topic.

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

Ouided Rouabhi: Thank you, Kim. As Kim mentioned, today we're going to be covering updates to the Breakthrough Devices Program Guidance that were issued on September 15. A link to the final guidance is provided here within the slides.

Our learning objectives for this session are to describe CDRH's strategic priority to advance health equity, to provide an overview of the Breakthrough Devices Program, including a review of the criteria for breakthrough device designation, and importantly, to describe the updates that were made to the Breakthrough Devices Program Guidance, including how the program may apply to certain devices that benefit populations impacted by health and/or health care disparities.

We'll first start with a bit of background on CDRH's strategic priority to advance health equity.

Let's first define the terms, health equity and health disparities, so that we all have a common understanding as we move forward. Using the definition from the Centers for Disease Control and Prevention, health equity is the state in which everyone has a fair and just opportunity to attain their

highest level of health. A related term is health disparities. It is often the metric by which we measure progress towards health equity. It is the preventable differences in the burden of disease or opportunities to achieve optimal health. In the United States, conversations around health equity and health disparities have often revolved around factors like race, ethnicity, sex, age, and geography, as well as other characteristics.

There are many examples of notable disparities associated with these characteristics, whether it be overall life expectancy, chronic health conditions, like high blood pressure, cancer, or diabetes, or reproductive outcomes, like infant mortality. We have often observed worse health outcomes in racial and ethnic minorities and those living in rural settings. These poor health outcomes are tragedies for individuals, for families, and for society as a whole.

The Center for Devices and Radiological Health is leaning forward and taking proactive steps to further advance health equity by exploring opportunities to bring care closer to where people live, work, learn, and play. Technology may help bridge the divide in health care outcomes experienced by many groups, helping to advance better health care, quality of life, and wellness for all. This strategic priority reflects our belief that no person should be left behind in health care.

We have a number of objectives associated with this strategic priority, which include empowering people with the information they need to make informed health decisions, facilitating the availability of and access to medical devices, reducing barriers to participation in the evidence generation process, and supporting innovative approaches and devices that address health disparities.

Consistent with this strategic priority, we believe the Breakthrough Devices Program can help support the development of technologies that address important gaps in equity. The recent guidance update clarifies how the program may be applicable to certain devices that benefit populations impacted by health and/or health care disparities, thereby promoting and advancing health equity.

Before discussing the updates themselves, I'd like to provide a brief overview of the Breakthrough Devices Program.

At a high level, the intention of the Breakthrough Devices Program is to provide patients and health care providers with timely access to devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. This voluntary program allows for expediting the development, assessment, and review of certain devices that meet the program eligibility criteria.

Sponsors of breakthrough designated devices benefit from the program features that can help achieve the goal of more timely patient access. Among those is the opportunity for interactive and timely communication. Sponsors of designated breakthrough devices are able to receive feedback from FDA more quickly and collaboratively. This allows them to move forward with the device development decisions more quickly, while being reassured that the data they plan to collect is consistent with FDA expectations.

Similarly, the program also aims to prioritize the review of marketing applications for designated devices, as well as aims to apply efficient and flexible approaches during review, such as enhanced

opportunity for postmarket data collection for devices subject to PMA approval. All the while, preserving the statutory standards for marketing authorization.

There are a few things to note from a regulatory context. First, this is a voluntary program created under Section 515B of the Food, Drug, and Cosmetic Act, which was enacted as part of the 21st Century Cures Act at the end of 2016, and later amended by the FDA Reauthorization Act of 2017 and the SUPPORT for Patients and Communities Act.

A guidance document describing the program's implementation was first issued in December of 2018. This guidance covered the program's principles, as well as the process for requesting breakthrough device designation and the features available to sponsors of designated devices. Since this webinar is only focused on the updates that have been made to the guidance, we won't be reviewing all of these topics today. But there is more information available on CDRH Learn, including a link to a previous webinar that was held at the time the original guidance was finalized.

Select updates to the existing Breakthrough Devices Program Guidance were proposed in a draft guidance in October 2022. There was a 60-day public comment period following, which FDA reviewed and addressed comments. The updates have now been incorporated into a final guidance, which was issued on September 15 of this year and is the subject of this webinar.

Moving on now to eligibility considerations. There are a few general eligibility considerations that a device must meet to be designated breakthrough. These requirements are outlined in statute and are unchanged with this guidance update. First, the program is only open to medical devices and device-led combination products. Second, devices seeking breakthrough device designation must be subject to future marketing authorization via the PMA, De Novo, or 510(k) pathways.

Devices that are exempt from these marketing pathways would not be eligible for the program. Lastly, the device should meet the specific criteria outlined in the statute, including fully meeting Breakthrough Device Criterion 1 and one of the subparts of Breakthrough Device Criterion 2.

The first criterion requires that the device provides for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions. Most of the updates that we'll discuss today regard clarifications to this criterion.

The second criterion requires that the device in its proposed indication meet at least one of the following subparts in Criterion 2. Either that the device represents a breakthrough technology, meaning that the device represents a novel technology or novel application of an existing technology that has the potential to lead to a clinical improvement, or no approved or cleared alternatives exist, or that the device offers significant advantages over existing approved or cleared alternatives, including the potential to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patients' ability to manage their own care, or establish long-term clinical efficiencies.

And lastly, that the device availability is in the best interest of patients. We won't be specifically covering Criterion 2 today, but our guidance document does talk about considerations for these subparts in more detail.

Moving on now to the recent updates finalized in the Breakthrough Devices Program Guidance.

This slide provides a summary of the updates, which we'll be discussing. The updated guidance clarifies considerations in designating devices, including eligible devices that benefit populations impacted by health and/or health care disparities.

It also clarifies the availability of the program for certain non-addictive medical products intended to treat pain or addiction, as well as clarifies existing policies regarding disclosure of breakthrough designated devices. It's important to keep in mind that the program designation criteria and goals are not changing with these updates. Additionally, the sections of the guidance that were not affected by the updates remain unchanged from the 2018 guidance.

To better understand the context for these updates, let's first consider what the guidance already stated when it comes to considerations for Criterion 1. Because decisions on requests for designation are made prior to marketing authorization and a complete clinical data set is not required and may not be available at the time of designation, FDA considers whether the sponsor has demonstrated a reasonable expectation that the device could provide for more effective treatment or diagnosis of the disease or condition identified in the proposed indications for use.

Reviewers take into consideration whether the sponsor has demonstrated a reasonable expectation of technical success, meaning that we reasonably expect the device can be built and function as intended, as well as clinical success, meaning that a functioning device could more effectively treat or diagnose the identified disease or condition.

The original guidance described that mechanisms for demonstrating a reasonable expectation of technical and clinical success could include literature or preliminary data, including bench, animal, or clinical data.

In the guidance updates, we further clarified considerations for Criterion 1. First, we recognize that the level and type of evidence needed to determine whether a device is reasonably expected to provide for more effective treatment or diagnosis may vary depending on different factors. These include the intended use of the device, its technology and features, and the available standard of care alternatives. For example, if you have a device intended to be used for a condition that has several treatment options that are known to be very effective, then the level and type of evidence needed to demonstrate that your device is expected to be more effective for the purposes of breakthrough designation may be greater than that needed for a device intended for a condition that has no treatment options available or alternative options that aren't very effective.

The guidance updates clarify that when evaluating the first criterion, FDA considers the totality of information regarding the proposed device, its function, potential for technical success, potential for clinical success, potential for a clinically meaningful impact, and its potential benefits and risks. And the determination of whether a device is reasonably expected to provide for more effective treatment or diagnosis is based upon all of these factors.

As we mentioned earlier, another important purpose of these updates is to clarify how the program may be applicable to certain devices that benefit populations impacted by health and health care disparities. Disparities can occur across diverse populations and are impacted by many factors, including race, ethnicity, socioeconomic status, age, sex, and location, among others.

Addressing health and health care disparities is not only important for achieving health equity, but also for improving the overall quality of life and health outcomes for all patients. We recognize that there is a public health need for innovative technologies that help to reduce barriers to achieving health equity and that help to improve health outcomes across diverse populations.

The updated guidance clarifies that when assessing eligibility for the Breakthrough Devices Program using the statutory designation criteria, FDA intends to consider technologies and device features that may help to address health and/or health care disparities and promote health equity by providing for more effective treatment or diagnosis in populations that exhibit these disparities. And we've created a new subsection of the guidance specifically aimed at describing considerations related to reducing health and health care disparities.

It's important to acknowledge that health and health disparities exist and occur across many dimensions and that different factors may influence treatment response and outcomes. Treatment outcomes may differ by race, ethnicity, sex, age, disability, and/or other factors. And for some diseases, the pathophysiology, clinical features, and response to treatment may also be impacted. For example, differences in health outcomes may exist for pediatric and geriatric patients due to age-related physiological changes.

Disparities can be exacerbated due to a lack of recognition of these differences, including implicit biases. Disparities may also occur when there is a lack of devices designed to effectively diagnose or treat conditions in a manner that addresses these differences.

The guidance updates clarify that the Breakthrough Devices Program can be used to help provide more timely access to devices that address the unmet needs of populations that may experience health and health care disparities. When evaluating if there's a reasonable expectation that the device may provide for more effective treatment or diagnosis as compared to the current standard of care, FDA considers technologies and device features tailored to address characteristic differences, including the device's potential to be more effective in certain populations. Examples of characteristic differences include those arising from social factors, phenotypic variations, pathophysiology, and/or response to treatment, among others.

Similarly, health and health care disparities may also arise in populations impacted by life-threatening or irreversibly debilitating diseases or conditions that are rare. In some cases, patients living with these rare diseases or conditions may have limited diagnostic and treatment options. The updated guidance reflect FDA's consideration of devices tailored to address unmet needs in these populations when evaluating Criterion 1.

It's important to keep in mind that the marketing pathway eligibility requirements still apply, meaning that in order for a device to be eligible, the expected marketing pathway should be a PMA, 510(k), or De Novo. Sponsors should only request a breakthrough device designation if they intend to pursue one of these marketing pathways. Other marketing pathways, for example, a Humanitarian Device Exemption, or HDE pathway, are not eligible for consideration under the Breakthrough Devices Program.

The updated guidance also discusses considerations related to accessibility to quality health care. We recognize that certain barriers, such as inequities in the availability of medical care, may prevent

underserved populations from receiving medical treatment or diagnosis. And often, the benefit of a device cannot be realized due to this lack of accessibility.

The guidance updates clarify that new devices that have the potential to offer a clinically meaningful impact through improved accessibility may provide a significant benefit to patients by, for example, including user features that are adaptable or more easily used by diverse populations, or allow for use in more diverse settings.

As we described earlier, when determining whether a device is reasonably expected to provide for more effective treatment or diagnosis, FDA considers the totality of available information regarding the device, including its potential for clinically meaningful impact and its potential benefits and risks. Therefore, when evaluating the first breakthrough criterion, FDA intends to consider technologies and device features that could allow for improved accessibility when evaluating if there's a reasonable expectation that the device may provide for more effective treatment or diagnosis as compared to the current standard of care.

For example, improved accessibility of the device may support that the device is reasonably expected to be more effective if there's information supporting its use in diverse settings, such that a patient population with limited or no available options may have improved adherence to a prescribed medical regimen.

In addition to these updates related to health and health disparities, the guidance has been updated to highlight the availability of the Breakthrough Devices Program for certain non-addictive medical products to treat pain or addiction consistent with FDA's obligations under the SUPPORT for Patients and Communities Act.

Lastly, the guidance updates have clarified FDA's policy related to timing of disclosure of designated breakthrough devices. FDA, generally, will not disclose the existence of requests for breakthrough device designation and/or decisions on such requests, except in certain circumstances when that designation has been previously publicly disclosed or acknowledged by the sponsor of the breakthrough device designation request.

Once a designated breakthrough device obtains marketing authorization for an indication consistent with its breakthrough device designation, FDA intends to publicly disclose its breakthrough device designation status for that indication for use. Currently, we maintain a list of market authorized breakthrough devices on our Breakthrough Devices Program webpage, which you can see an example of on this slide.

If a designated breakthrough device receives marketing authorization for an indication other than the indication covered by its designation, it is not considered a market authorized breakthrough device and would not be disclosed as such.

Before concluding the presentation, I wanted to mention that within the slide deck, we've included links that you can reference to access the mentioned resources.

In summary, the Breakthrough Devices Program is intended to provide patients and health care providers with timely access to breakthrough devices. FDA has released an updated guidance to clarify

designation considerations, including the Agency's intention to consider technologies aimed at reducing health and health care disparities and devices intended to treat pain and addiction, and the timing of breakthrough designation disclosure. We intend for these guidance updates to promote innovation of technologies that address health and health disparities as a part of CDRH's strategic priority to advance health equity.

That brings us to the end of our presentation. I'll now turn it back over to Kim.

CDR Kim Piermatteo: Thanks, Ouided, for your presentation. At this time, we will now transition to our interactive question and answer segment. We have gathered a panel of subject matter experts, in addition to Ouided, to help you better understand and get clarity on what we intend in this final guidance.

So joining Ouided today on our panel is Dr. Brittany Caldwell, Assistant Director of the Partnerships to Advance Innovation and Regulatory Science team within the Division of All Hazards Response, Science, and Strategic Partnerships in the Office of Strategic Partnerships and Technology Innovation, or OST, in CDRH. Also joining Ouided is Samantha Collado, Regulatory Policy Analyst in CDRH's Office of Policy, and Megha Reddy, Regulatory Advisor on the Regulation, Policy and Guidance staff within CDRH's Office of Product Evaluation and Quality, or OPEQ. Thank you all for joining us and participating on our panel today.

Before we begin, I'd like to go over how we will manage this segment. So to ask a question, please select the Raise Hand icon, which should appear on the bottom of your Zoom screen. If you previously raised your hand earlier in the webinar, we did lower your hand. So those of you that have currently raised your hand, that is fine. But if you raised it at the beginning of the webinar, we did lower your hand.

So once you raise your hand, though, I will 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. And we also appreciate that you may have a very specific question involving your device or specific scenario. However, we might not be able to answer such specific questions. Therefore, we will try to frame a broader response based on what's described in the final guidance. After you ask your question, please lower your hand. If you do have another question, please feel free to 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 some of your questions, I'd like to welcome our newest panelists with a few questions we have received about this final guidance. For our first question, I'll be directing that to Brittany. Brittany, the question is, do the updates to the final guidance include considerations for how social determinants of health may contribute to health disparities?

Brittany Caldwell: Thanks for the question, Kim. Social determinants of health are the conditions in the environments where people are born, live, learn, work, play, and age that affect a wide range of health, functioning, and quality of life outcomes and risk. Social determinants of health are very important and we recognize that there may be overlapping considerations between social determinants of health and health equity, such as health care access and quality.

However, these variables are often difficult to measure. They may impart their impacts over protracted periods of time and may have interactions with each other, as well as other factors. Hence, it is challenging to measure or account for all of these effects in a clinical study that is designed to evaluate the safety and effectiveness of an investigational medical product.

If a sponsor believes that their proposed device provides a benefit to patients that may help address health and health care disparities consistent with the considerations outlined in the guidance updates, we would encourage them to apply for the program.

CDR Kim Piermatteo: Thank you, Brittany. Now for our next question, I'll be directing that to Samantha. Samantha, the question is, as mentioned in the presentation, the guidance has also been updated to reflect FDA's consideration of devices tailored to address the unmet needs of patients with rare diseases and conditions. Does this mean that devices subject to the HDE pathway are now eligible for breakthrough?

Samantha Collado: Hi, Kim. Thanks so much for the question. That's a really good one. As discussed, in order for a device to be eligible for the breakthrough designation, the expected marketing pathway should be a PMA, 510(k), or De Novo. Other marketing pathways, such as HDE, are not eligible for consideration under the Breakthrough Devices Program. However, sponsors of devices planning to pursue a PMA, De Novo, 510(k), for devices intended to treat rare diseases, regardless of whether they be, otherwise, eligible for HDE pathway, are eligible for breakthrough device designation.

CDR Kim Piermatteo: Thanks, Samantha. Now for our next question before we get to our questions from you, I'll be directing that to Megha. Megha, the question is, it's important that populations impacted by health and health care disparities are provided with quality devices. How does inclusion in the Breakthrough Devices Program impact the evidence needed for marketing authorization?

Megha Reddy: Thank you, Kim. So FDA aims to facilitate the development of devices designed to address health inequities, but we must do so in a manner that ensures that commercially-available devices are safe and effective. The Breakthrough Devices Program features are designed to expedite the availability of breakthrough designated devices, while preserving the statutory standards for marketing authorization. In other words, the breakthrough designation does not impact the standard for marketing authorization, and marketing submissions for breakthrough designated devices are held to the same standards as similar devices that do not have breakthrough designation.

As part of FDA's benefit-risk determination for devices, FDA may consider the amount and nature of data that may be collected in the postmarket setting rather than premarket, and the extent of uncertainty that may be appropriate in the benefit-risk profile at the time of approval. FDA will consider the unmet need or health disparity addressed by a breakthrough designated device when deciding the degree of acceptable uncertainty and appropriate pre/postmarket balance in data collection for a marketing authorization of a breakthrough designated device. Thank you.

CDR Kim Piermatteo: Thanks, Megha. Alright, we will now take our first live question. Our first live question is coming from Eric. Eric, I have unmuted your line. Please unmute yourself and ask your question.

Eric Chen: Great. Thanks. Thanks for that, Kim, and thanks for FDA for putting on this great webinar to provide industry with an update on the Breakthrough Devices [INAUDIBLE] Program. So my question surrounds the expansion of this with regards to health and health disparities, as well as non-addictive medical products to pain.

So at the end of the day, FDA still requires, whether or not these devices are intended to benefit this population, that you have to meet the first criteria, which is, the device has to be treating or diagnosing a life-threatening or irreversible debilitating disease or condition. So just want to make sure that the disease or condition still has to be life-threatening or irreversible debilitating in order to qualify for breakthrough, regardless if you're planning to have the technology used to impact health disparity or non-addictive pain. Is that correct?

CDR Kim Piermatteo: Thanks, Eric. I'm going to turn it over to Ouided to provide you a response.

Ouided Rouabhi: Thank you, Kim, and thanks, Eric, for that great question. So in short, yes. In order for a device to be eligible for the Breakthrough Devices Program, the disease or condition that the device is intended to diagnose or treat does need to be either life-threatening or irreversibly debilitating.

And that is because the eligibility criteria or the designation criteria are outlined in the breakthrough devices statute, and they do require that the device has to be intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition.

Eric Chen: Thank you for that clarification.

CDR Kim Piermatteo: Thanks, Eric. Thanks, Ouided, for your response. Our next question is coming from Rebecca. Rebecca, I have unmuted your line. Please unmute yourself and ask your question.

Rebecca Gilbert: Hi. Thanks. I just have a clarification question regarding some of the health equity standards and disparities for designation and just kind of the way that FDA ends up weighing a decision.

So if you have a device that potentially offers a better treatment or diagnosis for a particular population that is perhaps victimized by some type of health disparity currently, but you don't necessarily have data that shows that it provides a better treatment or diagnosis for a large percentage of just the general population, how does FDA weigh that decision?

You know, it's perhaps not something that is quite Humanitarian Device Exemption qualified. Like, it's not that specific. But as far as receiving the designation, and then ultimately, how a company crafts their indications for use, not wanting to carve out potentially too specific of a population, but knowing that their device potentially offers particular benefits to a more limited population.

CDR Kim Piermatteo: Thanks, Rebecca. Ouided, would you like to provide a response?

Ouided Rouabhi: Thank you, Kim. And again, great question, Rebecca. So I guess to put it plainly, when assessing eligibility for breakthrough device designation, we're really looking at the device and its proposed indications for use.

And so when looking at that criteria, we are considering, like for example, Eric clarified that the disease or condition is life-threatening or irreversibly debilitating, and we're assessing, when it comes to the first criterion, that device's potential to be more effective as compared to the current standard of care.

Now with these new updates to the guidance, what we've done is clarified FDA's interpretation of what it means to be more effective. And we recognize that with available standard of care alternatives, they might not be equally effective in all patient populations. And so with these updates, we're clarifying that FDA may consider devices that are tailored to either address characteristic differences or improved accessibility that might help address health or health care disparities in certain populations when determining whether that device might provide for more effective treatment or diagnosis.

So in other words, when we're thinking about what it means to be more effective, we're looking also at whether the device can be potentially more effective in certain patient populations that are exhibiting health or health care disparities.

CDR Kim Piermatteo: Thanks, Ouided, for your response. Again, thanks, Rebecca, for your question. Our next question is coming from Shiven. Shiven I've unmuted your line. Please unmute yourself and ask your question.

Shiven are you able to unmute your line? Are you there?

Shiven: Yes, I was able to. Yes, I was able to unmute. My question is that, can the Agency comment on how and if Pre-Submissions are treated differently for a breakthrough designated device versus a non-breakthrough device? And the second question is, what is an acceptable cadence of Pre-Submission that the Agency would like to see for a breakthrough device?

CDR Kim Piermatteo: Thank you, Shiven for your question. Ouided or Megha, would you like to provide a response?

Ouided Rouabhi: Hi Kim, this is Ouided. I'm happy to provide a response.

CDR Kim Piermatteo: OK.

Ouided Rouabhi: So in terms of the first question, as to how breakthrough designated devices or interactions for breakthrough designated devices compare to requests for feedback that are submitted under a traditional Pre-Submission, so typically, interactions for designated breakthrough devices, feedback is provided on an expedited timeframe and there's also increased amount of interaction and collaboration from FDA. So we really intend for it to be a very collaborative and communicative process, so that FDA can work with the sponsor to reach resolution and provide feedback more quickly.

And I apologize. I think there might have been a second question in there, but I missed it.

Shiven: The second question was, what is the acceptable cadence of Pre-Submission that the Agency would like to see for a breakthrough device?

Ouided Rouabhi: So for this one, I think this is a bit of outside the scope of this current webinar. But I would encourage you to work with the review team assigned to your particular device to come up with an appropriate interaction strategy.

Shiven: Thank you so much.

CDR Kim Piermatteo: Thanks Shiven. Thank you, Ouided. Alright, our next question is coming from Joe. Joe, I have unmuted your line. Please unmute yourself and ask your question.

Joe Beggs: Hi, thanks. Are criteria 2B and 2C mutually exclusive?

CDR Kim Piermatteo: Thank you for that question, Joe. This is specific to the guidance. Ouided, would you like to provide a response?

Ouided Rouabhi: Yes, thank you Kim. And thank you Joe, for that question. So yes, typically, we would expect for a device to either fulfill 2B, meaning that there are no approved or cleared alternatives, or fulfill 2C, meaning that there are approved or cleared alternatives and this device provides significant advantages over existing approved or cleared alternatives.

Joe Beggs: OK. Sorry. Can I ask a follow up or should I—

CDR Kim Piermatteo: Yes, you can.

Joe Beggs: If we're pursuing a De Novo pathway that implies that there's no marketed device with our proposed indication for use, does that also preclude us from one of the criteria, which says that there are alternatives, but they're not sufficiently addressing the problem?

CDR Kim Piermatteo: Thanks again, Joe. Ouided, did you want to provide a follow up to that one?

Ouided Rouabhi: Yes. Thank you, Kim. And this is a bit outside the scope of our current webinar today, but just to give a quick response. So when we assess Criterion 1 and Criterion 2, we're looking at the current standard of care alternatives. And that standard of care alternative could include not just devices, but also other available medical products, including drugs and biologics.

And so if there are other available standard of care alternatives that this device might provide significant advantages over, just because there aren't available devices necessarily does not mean that there wouldn't be other available medical products. I can go into more detail. I think there could also just because there's-- just because it's De Novo doesn't necessarily mean that there aren't other devices out there that might still be considered standard of care.

But that is a bit outside the scope of today's webinar. So I would encourage you, if you do have follow up questions, to please reach out to the Breakthrough Devices Program mailbox. And that email address is BreakthroughDevicesProgram@fda.hhs.gov.

Joe Beggs: Thank you.

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

Paige Maness: Hi, can you hear me?

CDR Kim Piermatteo: Yes, we can.

Paige Maness: Excellent. Thank you for hosting this webinar and taking my question. So during the presentation, it was suggested that preliminary bench animal and clinical data may be submitted to support eligibility. And our most recent experience submitting a breakthrough aligns with the trend that FDA is looking for data that is derived from a more finalized device design.

However, per section 3C of the guidance, and as we previously discussed in another question, if you're going to pursue the breakthrough designation, you might want to wait and submit that prior to submitting other Pre-Subs.

So the question is, if some of the benefits of the program are best utilized during preliminary design and development, like the sprint discussions, the PDP, and the protocol agreement, and FDA is suggesting that we submit prior to other Pre-Submissions, can FDA comment on how to reconcile those benefits and suggestions with this desire for the finalized device data?

CDR Kim Piermatteo: Thanks, Paige. I'm going to turn it over to Ouided to provide you a response.

Ouided Rouabhi: Thank you, Kim. And again, great question, Paige. So one of the things that's been clarified with this guidance update is that the level and type of evidence may vary across different devices and device areas, and that can be due to a variety of different factors, including things like what that particular device is intended for, what other available standard of care alternatives it might be used for, what are the technological features of that particular device. And all of that might kind of help determine the level and type of evidence we're looking for when trying to determine whether that device has a reasonable expectation of technical and clinical success.

One thing that we've, importantly, also clarified in this guidance update is that when evaluating the first criterion, we'll consider the totality information regarding the proposed device, its function, potential for technical success, potential for clinical success, but then also potential for clinically meaningful impact and its potential benefits and risks. And it's really all of these factors that go into that determination of whether you've been able to demonstrate that your device would be expected to be more effective.

And of course, we recognize that devices have the most to benefit from the program when they do come in early on in development and there's program features that can be more useful when you're in those earlier stages of development and trying to determine what data collection expectations there are, what methodology to use, what testing to perform. Those sorts of questions. And our intention is for the device to be utilized in that way. But then we also recognize that depending on the particular device area, there might already be a plethora of devices that are already very effective. And so there might be potentially greater data expectations in those areas where there are existing devices and they are reasonably effective.

And you'd have to then demonstrate that your device is more effective than those existing devices versus, as we mentioned in the talk, if you're in a device area where there are very limited alternatives and/or alternatives that aren't very effective, then we might have lesser data expectations in that sense because there's just a greater amount of potential there.

Paige Maness: Thank you so much. That provides excellent clarity.

CDR Kim Piermatteo: Thank you, Paige, for your question. Thank you, Ouided, for the response. Our next question is coming from Abhi. Abhi I've unmuted your line. Please unmute yourself and ask your question.

Abhi Mukherjee: Hi, can you hear me?

CDR Kim Piermatteo: Yes, we can.

Abhi Mukherjee: OK. Thank you for this great webinar today. So my question is regarding a follow up to this previous question from Paige. So in terms of establishing the clinical success of the device for better outcomes, would FDA expect mostly like some type of clinical data, or providing devices, just bench testing or animal testing data would be sufficient?

What is the best timing to do this? Because if we are already going into a feasibility study and have to submit an IDE submission, in my mind, I think it is already much more development has happened. So I wanted to get FDA's thoughts on this process. Thank you so much.

CDR Kim Piermatteo: Thank you for that question. Ouided, would you like to provide a response?

Ouided Rouabhi: Yes. Thank you, Kim. And again, great question. So one thing that you want to keep in mind is that when thinking about clinical success, what we mean by that, as outlined in our guidance, is that a functioning device could more effectively treat or diagnose the identified disease or condition. But that doesn't necessarily mean that we need clinical data in order to demonstrate clinical success because we're only looking for a reasonable expectation of clinical success.

And in fact, the guidance actually says that we don't expect a final clinical data set at the time of breakthrough designation because, again, sponsors can really benefit from the program if they're able to come in earlier on in their device development and utilize the features of the program to come up with their clinical study protocol, for example, or to work with FDA to come to an agreement on a clinical study. It's great if you can come in earlier in device development, so that you are able to benefit from those features.

So there is no expectation that a device needs to have clinical data in order to be able to demonstrate a reasonable expectation of clinical success. Now with that said, you know, like we mentioned earlier, the level and type of evidence is going to vary depending on the specifics of your device. And so particularly, there could be certain clinical areas where some preliminary clinical data may be needed in order to demonstrate that reasonable expectation of clinical success. But again, it's not an across-the-board requirement.

Abhi Mukherjee: Thank you so much. That's very helpful.

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

Ryan Campion: Hello. Thanks for taking the question. I know we didn't dive into it in this webinar for Criterion 2. But if I had questions regarding Criterion 2, what is the best way to ask those questions in terms of qualification? Is there a process to follow akin to the Pre-Sub process to get clarification on qualification for criteria 2?

CDR Kim Piermatteo: Thank you, Ryan, for that question. I do know that question may be most appropriate for the breakthrough program mailbox. That's the one that we did mention earlier. I think, Ouided, it is BreakthroughDevicesProgram@fda.hhs.gov, correct?

Ouided Rouabhi: Yes, that is correct, Kim.

CDR Kim Piermatteo: OK. So Ryan, that would be the best avenue for that question. Alright, our next question is coming from Varun. Varun I've unmuted your line. Please unmute yourself and ask your question.

Varun Kapoor: Hi. Thank you. Can you hear me?

CDR Kim Piermatteo: Yes, we can.

Varun Kapoor: Great. So my question is for specific devices that are in line with IVDs or other diagnostics. If we are able to showcase, for example, the potential for earlier screening reducing economic burden in, obviously, later stage patients who have to continuously spend on medical costs and other procedures and treatments because of the lack of a diagnosis, that we would be able to facilitate with our device, would that meet the requirements for some of the new aspects around health inequities?

And I'm tying that, really, to socioeconomic statuses for patients who would benefit from an earlier diagnosis in groups that, obviously, are less able to afford care.

CDR Kim Piermatteo: Thanks, Varun. I'm just going to open it up to the team. I think this is a specific question. But does anyone on the team want to provide a response?

Megha Reddy: Sure, I can take that, Kim. Varun this is a specific question. So I think we'd be able to help you best if you just reached out to the breakthrough mailbox that Ouided had mention earlier. That way we can look into the details of your specific product and provide tailored feedback. Thank you.

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

Alright, we're going to move down to the next stakeholder. The next person I'm calling on is Divya. Divya I have unmuted your line. Please unmute yourself and ask your question.

Divya Chander: Hi. Thanks. I just wanted to clarify that you can take advantage of this process before you actually have your MDP as long as you have data that demonstrates the device is of value to this disadvantaged group based on literature? And that FDA will then help with the preparation and design of clinical trial, appropriate documentation, to expedite review then.

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

Ouided Rouabhi: Hi, Divya, thank you very much for that question. Yeah. So in general, if a sponsor feels like they have a device that might meet the breakthrough designation criteria and that they potentially have some supporting data or literature to help demonstrate that reasonable expectation of technical and clinical success, then we would encourage them to apply for the program, and the review team at the time will assess eligibility for that device, including if there are any considerations related to health disparities.

CDR Kim Piermatteo: Thanks, Ouided, for that response. Our next question is coming from Bijan. Bijan I've unmuted your line. Please unmute yourself and ask your question.

Bijan Tadayon: Hello. Can you hear me?

CDR Kim Piermatteo: Yes, we can.

Bijan Tadayon: OK. Hi. That was a great presentation. Really appreciate that. How long does it take when you apply for such a thing, how long does it take to get the approval? Like, average. Like, a minimum, maximum. What's the range of the-- how many months or years is going to take between minimum to maximum?

CDR Kim Piermatteo: Thanks Bijan for that question. I do think that that is going to have-- it's going to depend. But does anybody on our team want to provide sort of a general, overarching response?

Ouided Rouabhi: Hi, Kim. This is Ouided.

CDR Kim Piermatteo: OK.

Ouided Rouabhi: So when applying for breakthrough device designation, the breakthrough devices statute does actually specify that FDA will provide a decision within 60 calendar days. So within 60 calendar days from you submitting your breakthrough device designation request, FDA will provide a decision on that request. Typically, we do intend to interact with sponsors sooner than that if there are questions related to the submission and there are any requests for additional information. But do expect a response by day 60.

Bijan Tadayon: OK. So it's pretty fast. Thank you.

CDR Kim Piermatteo: Thanks, Bijan for your question. And thanks, Ouided, for your response. Our next question is coming from Lindsay. Lindsay, I have unmuted your line. Please unmute yourself and ask your question.

Lindsay: Hi. Thank you very much for the webinar. My question builds on a previously asked question. For a designated breakthrough device, what is the timeframe a sponsor should expect to receive feedback for sprint discussion? Because the guidance explains they will receive priority review and gives examples ranging from day 7 to 45, but it does not firmly outline a date by when FDA should be received.

So our experience has been this is typically coming between day 45 and 70. As a sponsor, it's making it difficult to plan timelines and projects. And so I was wondering if you could comment. Should we be using this firm 70-day length, which is coming from the Q-Sub guidance, or is day 45 typically what I should be expecting? Thank you.

CDR Kim Piermatteo: Thanks, Lindsay. Ouided, I'm going to turn it over to you.

Ouided Rouabhi: Thanks very much, Kim. So Lindsey, you're absolutely correct that, as mentioned in the guidance, we do intend to prioritize regulatory submissions for designated breakthrough devices, including interactions for breakthrough designated devices, which would include things like sprint discussions. So they are expected to provide feedback on a timeframe earlier than the typical Pre-Submission timeline of 70 days.

You know, typically, that might be day 45, as an example that's given in the guidance. But really, that can vary depending on the scope of the interaction. Keep in mind that for sprint discussions, in particular, we really do intend for that to be a very interactive and collaborative process.

And so the goal is that throughout that review period, unlike in a Pre-Submission where you just receive written feedback towards the end of the review, with the sprint discussion, the goal is really to be interactive throughout that review period and to have those back and forth question and answer sessions with the sponsor and FDA, so that they can hopefully come to a resolution on whatever that particular topic of feedback is.

Lindsay: Thank you.

CDR Kim Piermatteo: Thanks, Lindsay, for your question. And thank you, Ouided, for the response. Our next question is coming from Luke. Luke, I have unmuted your line. Please unmute yourself and ask your question.

Luke Schwartz: Hi. Thanks so much for providing this forum. My question is with regards to intellectual property and if there is still some component of that that is outstanding, patents that haven't been obtained. Does the FDA have any guidance on whether breakthrough device submission should be made with that outstanding? I guess, what is the measure of protection of trade secrets once you make that submission?

CDR Kim Piermatteo: Thank you Luke for your question. That does sound a little bit of outside of today's scope. I'm not sure-- maybe Samantha, if you wanted to provide some feedback on what is considered trade secret and how we handle those when it comes to breakthrough device designations.

Samantha Collado: Alright. I think that's a fair question. I would recommend you writing into the breakthrough devices program email box. Yeah. I do appreciate the question, though.

Luke Schwartz: OK. Thank you.

Ouided Rouabhi: Sorry to cut you off there. Maybe I could add another quick comment related to that. So generally speaking, breakthrough device designation requests are considered confidential. They are submitted as Q-Submissions and we generally do not disclose the existence of those designation requests or our decisions on them. So that is something to bear in mind as well.

Luke Schwartz: OK. Thank you very much.

CDR Kim Piermatteo: Thanks, Luke. Thanks, Ouided and Samantha. Alright, we have time for one more quick question and, hopefully, a quick response. The next hand raise is coming from a number. It's z0046srv. I have unmuted your line. Please unmute yourself and ask your question.

Paul Speidel: Hi. My name is Paul Speidel. Thanks so much for taking my question. It's a follow up to some responses you guys have made. It sounds like if you want to engage with FDA before filing the breakthrough application, you'd go through the mailbox. Does that typically lead to conversations after you've gone through the mailbox, or have other people reached out to FDA and had conversations separate from the mailbox prior to their filing?

CDR Kim Piermatteo: Thank you. I didn't quite get your name. If you could just repeat that for the record, and then I think Ouided is going to provide you a response.

Paul Speidel: Sure. My name is Paul Speidel.

CDR Kim Piermatteo: Paul Speidel. Thank you. Ouided.

Paul Speidel: Thank you.

CDR Kim Piermatteo: Yeah. Ouided, I'm going to turn it over to you.

Ouided Rouabhi: Yeah, Thanks very much, Kim. And thank you, Paul, for that question. So generally speaking, if you have questions related to the Breakthrough Devices Program our mailbox is a great point of contact. It's, again, BreakthroughDevicesProgram@fda.hhs.gov. Particularly, for those more general questions about breakthrough program processes or policy type questions that are more general, we're happy to help answer.

Specific questions about our devices eligibility may not be able to be accessed through a simple email since, again, we haven't yet reviewed the designation requests and all of the supporting information and rationale and justification that come along with that in order to determine whether a specific device may be eligible. But the mailbox is a great initial point of contact.

I would also say, if you have already had previous interactions with FDA, for example, through an earlier Pre-Submission, and you already have a particular review team that you've been assigned to, you can always consider reaching out to your lead reviewer as well and considering if they might be able to help address some questions or if they would, for example, suggest a pre-submission to help provide additional feedback.

Paul Speidel: Thank you very much. That was really helpful.

CDR Kim Piermatteo: Thanks Paul for your question. And thank you, Ouided, for your response. With that, that will wrap up our question and answer segment. I want to thank you all for your questions. And I'd now like to turn it over to Ouided for her final thoughts for today. Ouided.

Ouided Rouabhi: Thank you very much, Kim. And thanks, again, to everyone for the great questions today. As we wrap up, I just wanted to mention that, consistent with CDRH's strategic priority to advance health equity, we really believe that the Breakthrough Devices Program can help support the development of technologies that address important gaps in equity. And we really encourage device sponsors that may have eligible devices to consider applying for the program.

CDR Kim Piermatteo: Thank you Ouided, for those final thoughts, as well as your presentation for today. I'd also like to thank Brittany, Samantha, and Megha for participating on our panel.

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, "Clinical Studies/Investigational Device Exemption or IDE."

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

As we mentioned throughout the webinar, if you have questions about this guidance document, please contact CDRH's Breakthrough Devices Program at BreakthroughDevicesProgram@fda.hhs.gov. If you have additional questions about today's webinar, feel free to reach out to us in DICE at DICE@fda.hhs.gov.

Lastly, we hope you are able to join us for a future CDRH webinar. And a listing of all of our upcoming webinars can be found via the link provided on the bottom of this slide at www.fda.gov/CDRHLearn.

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

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