FDA Webinar: Breakthrough Devices Program Final Guidance
Moderator: Irene Aihie
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1:00 pm ET

Coordinator: Welcome and thank you for standing by. At this time all lines are in a listen-only mode. During the question and answer session please press Star 1 on your touchtone phone.

I would also like to inform parties that today's conference is being recorded. If you have any objections you may disconnect at this time. Now I'd like to turn today's conference over to Miss Irene Aihie. Thank you ma'am, you may begin.

Irene Aihie: Hello and welcome to today's FDA Webinar. I am Irene Aihie of CDRH's Office of Communications and Education. On December 18, 2018 the FDA issued the final document that outlines program policies, features, and the process for implementing the Breakthrough Devices Program.

The Breakthrough Devices Program is one of the FDA's initiatives that promote patient access to innovative and potentially safer new therapies and diagnostics for life-threatening or irreversibly debilitating diseases or conditions.

The goal of the program is to provide patients and healthcare providers with timely access to devices that treat or diagnose a life-threatening or irreversibly debilitating condition. These devices offer new ways to treat or diagnose a disease, have significant advantages over existing treatment alternatives, or provide another public health benefit.

Today, Maureen Dreher, a policy analyst here in CDRH, will present an overview of the Guidance Document. Following the presentation, we will open the line for your questions related to information provided during the presentation.

Additionally, there are other Center subject matter experts here with us today to assist with the Q&A portion of our Webinar. Now, I give you Maureen.

Maureen Dreher: Thank you all for calling into today's Webinar and thank you for your patience as we get the Webinar up and running. As was mentioned by Irene I'll be presenting on our Breakthrough Devices Guidance which was published in final in December of 2018.

This is the agenda for what we'll discuss today. We'll begin with a background for the program and then move into the scope and structure of the final guidance.

I'll highlight some of the differences between the draft and final version and discuss the regulatory framework for this program as well as some of the procedural and policy implications for you as a sponsor and us as FDA. We'll reserve some time at the end for questions.

Our primary objective today is to provide you with an understanding of the following elements for the program. First, I'd like to provide you with the

purpose and scope for the Breakthrough Devices Program and we'll discuss the Breakthrough Devices criteria as well as what obtaining a Breakthrough Device Designation means for a sponsor and FDA Review Team.

We'll also discuss the administrative processes for submitting a Breakthrough Devices Designation Request and how to engage with FDA after a designation has been obtained. Many of the terms and definitions I'll be defining as we go along through the presentation, but here are a few additional ones which you should be familiar with up front.

Q-Submissions are a regulatory submission mechanism to request different types of interaction with FDA. These include requests for feedback regarding potential or planned medical device submissions, as well as requests for certain formal determinations that are not standalone marketing submissions or research authorizations. Some examples of Q-Submissions -- which you may already be familiar with -- include pre-submissions as well as study risk determinations.

The second term that you'll see in the presentation is an investigational device exemption or IDE. This is a mechanism to request approval for a significant risk clinical study of an unapproved device or unapproved use of a device.

And finally, the last abbreviation I have on this slide is the FD&C Act which is an abbreviation for the Federal Food Drug and Cosmetic Act.

I'll begin with some context for the Breakthrough Devices Program. Several years ago CDRH put out a Mission and Vision Statement that patients in the US would have access to high-quality, safe, and effective medical devices of public health importance first in the world.

To support this vision we initiated several programs and regulatory approaches which include early feasibility studies, increases in patient engagement, and increases in the use of real-world evidence, as well as the case for quality. The program which I'll be talking about today is our Breakthrough Devices Program and is aligned with many of these initiatives to support CDRH's Mission and Vision.

These programs will provide sponsors with a toolkit of options that they can utilize for advancing their device development depending upon their own unique needs and the stage of development of the device.

The Breakthrough Devices Program has several important predecessor programs, including the Innovation Pathway and the Expedited Access Pathway -- or EAP -- Program.

In particular, the EAP Program which we implemented through a final Guidance Document back in 2015 was designed to expedite the review of certain devices for treating life-threatening or irreversibly debilitating conditions that addressed unmet clinical needs.

In late 2016 Congress then passed the 21st Century Cures Act, which gave FDA the authority to establish a program for expediting the development and review of certain devices which represented breakthrough technologies. This became our Breakthrough Devices Program and it's now codified in Section 515B of the Food Drug and Cosmetic Act.

About a year later in 2017 we issued a draft Guidance document on the Program which was published and final on December 18, 2018. This Guidance Document clarifies the policies and procedures for implementing The Program and how we intend to operate.

Due to the overall consistency of vision and interpretation of the eligibility criteria for inclusion in Breakthrough with the prior EAP Program, we've now considered device which were accepted into EAP to also have Breakthrough Devices Designation and today this Breakthrough Devices Program has superseded EAP.

The ultimate purpose of this program is to help patients have more timely access to important medical devices than they would have otherwise had. The Device Development Pathway to an FDA Marketing Authorization can be a long one and some unexpected challenges we recognize can occur along the way.

However, with the Breakthrough Program, FDA commits to expediting device development and review for certain devices that meet our program's statutory criteria. We intend to accomplish this through working with sponsors in order to define with them a roadmap from the time they enter the program which may be early in their development through to the FDA Marketing Authorization.

And we do this through a collaborative and interactive approach which enables sponsors to address challenges in an efficient manner and gives them a transparent development process.

This is our program definition: the Breakthrough Devices Program is a voluntary one 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.

This program was intended to help patients have more timely access to these devices by expediting their development, assessment, and review while preserving the statutory standards for premarket approval, 510(k) clearance, and De Novo marketing authorization in a manner that's consistent with the Agency's mission to protect and promote public health.

There are really two main phases to the Breakthrough Program: it begins with a sponsor submitting a Breakthrough Designation Request to the Agency for review. If we grant that designation, the sponsor may then utilize new or special mechanisms for obtaining FDA feedback on their device development.

Sponsors with breakthrough devices can also utilize more traditional mechanisms for obtaining FDA feedback, like a Pre- Submission. Finally, the sponsor also utilizes a standard regulatory mechanism such as an IDE or a Marketing Submission for their device.

It is important to note that participation in the Breakthrough Devices Program does not change the requirements for approval of an application under an IDE if a significant risk clinical study is needed for the device. Nor does participation in the Breakthrough Devices Program change the requirements for marketing authorizations under a pre-market approval, a pre-market notification, or a De Novo classification pathway.

For granted breakthrough devices, this designation does track with the device for any subsequent regulatory submission. And it does afford it prioritized review as well as other benefits. If that designation request is denied, the traditional pathways are still available to obtain FDA feedback and for obtaining a marketing authorization in the future.

I'm going to shift a little bit now into some details regarding the guidance. The Breakthrough Devices Program Guidance summarizes the policies under which the Program will operate. And it spends a significant amount of time clarifying the administrative processes used to facilitate review of Breakthrough Device Designation Requests.

The guidance also provides an overview of options for obtaining FDA feedback to support device development.

In response to public comment on the draft Guidance we revised the structure of it to be more consistent with the chronology for how sponsors would enter the program and utilize its features.

We also clarified the medical products that are eligible for the program as well as the policies and procedures for obtaining FDA feedback following a Breakthrough Designation.

The Guidance is structured in a manner that's similar with many other FDA Guidance Documents and -- again -- aligns with the chronology that a sponsor may utilize the program. It begins with introduction and background for the program and discusses the overall problematic principles and policies for which we intend to operate.

The guidance document describes the components of Designation Request and includes a description of the statutory criteria for enryt into the program and what our review considerations for that are. The Guidance Document also describes the subsequent regulatory mechanisms that are available for obtaining feedback and granted breakthrough devices.

Next, we'll spend some time discussing the overall eligibility for the Breakthrough Devices Program. This program is available for medical products that are regulated as devices. Therefore, medical devices and device-led combination products are eligible.

Devices eligible for The Program must be subject to a marketing authorization by a pre-market approval, or PMA, a De Novo, or a 510(k). Additionally, the device must be determined to meet the breakthrough criteria specified in Section 515B of The Act. And on the next couple of slides we'll first provide that statutory criteria as they appear in The Act and then we'll get into more of our review consideration for them.

This is the first breakthrough criterion. The criterion states that a breakthrough device provides for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or condition.

Additionally, a device -- in order to be considered breakthrough -- must meet one of the following of the following subparts in Criterion 2.

Option A, it represents a breakthrough technology. Option B, there is no approved or cleared alternative. Option C, if an approved or cleared alternative exists the device needs to offer a significant advantage, such as reducing or eliminating the need for hospitalization, improving a patient's quality of life, facilitating a patient's ability to manage their own care, or establishing long-term clinical efficiencies.

Or, Option D, the availability of the device is in the best interest of patients. So, we're going to break these criteria down now a little bit more specifically and discuss our review considerations.

We'll begin with Criterion 1. In assessing whether a device provides for a more effective treatment or diagnosis of a life-threatening or irreversibly debilitating disease or condition, we consider if that condition is first life-threatening or irreversibly debilitating. This is an important part of the overall criterion and sponsors should include a justification for it in their application package.

We then consider if there is a reasonable expectation that the device could provide for more effective treatment or diagnosis relative to current standards of care in the US. And in order to make this evaluation, we consider different types of preliminary data. This may include non- clinical data like chronic animal studies, as well as literature analyses and scientific rationales.

Preliminary clinical data to support this criterion can certainly be used -- and it can be helpful -- but we don't require it outright.

In assessing Criterion 2 we also look at all of the subparts of this criterion to determine if a device meets it overall.

In Criterion 2A, we're considering whether or not the device represents a breakthrough technology. And to do that, we think both about the technological advances that are very novel, or if they represent a new use of an existing technology.

We also consider whether or not the device has potential to lead to clinical improvement. So, we're considering both technological and clinical features of the device in this subpart to Criterion 2.

In Criterion 2B, we evaluate whether or not there is an approved drug, biologic, or device for the same indication that's consistent with standard of

care. For Criterion 2C, we consider whether there is a potential for significant advantages in how the device is proposed to be used.

This includes looking at specific examples within the statue, which are reducing or eliminating the need for hospitalization, improving the overall patient quality of life, facilitating their ability to manage their own care, or establishing some long-term clinical efficiencies.

In Criterion 2D, we consider whether the availability of the device is in the best interest of patients at the time of the possible designation. So, what we're looking at here is whether the device will provide for some other specific type of public health benefit.

We have several examples of how a device might meet this subpart of the criterion in the Guidance Document. And two of them that I'd like to highlight here include the potential for the device to address a known failure mode or if it may be offering a benefit for a subset of patients who are unable to tolerate other available therapies.

Now, let's shift into some more of the policies and procedures for actual operation of the Breakthrough Devices Program. The primary principles for the Breakthrough Devices Program are derived from specific (unintelligible) that are in Section 515B of The Act. And that's where this program is overall described.

A hallmark of The Program is interacting and timely communication during the submission review and between submissions. So, overall this designation comes with a high level of review team support and senior management involvement. There are also opportunities for engaging external experts

during the review, not only at the designation request but also at subsequent submissions.

Breakthrough devices also receive prioritized review for any subsequent regulatory submission. And that includes any key submission, IDE, or marketing submission that comes in.

Finally, The Program provides for some enhanced opportunities when applying pre/ post-market balance of data collection or coming up with a flexible and efficient clinical study design.

There's also the opportunity for sponsors with breakthrough devices that are PMA to have an expedited Manufacturing and Quality Systems Compliance review.

So, I'm going to shift a little bit now into more of the administrative procedures for Breakthrough Device Designation Requests.

As a sponsor, if you're interested in having your device designated as a breakthrough device, you would submit what's called a Designation Request for Breakthrough Device Q-Submission. It's important to note that this submission is distinct from other types of Q-Submissions. It's its own type and it is not a pre-submission -- it is different from a pre-sub.

A Designation Request Q-Sub should include the following elements - and I should tell you these are also outlined in Appendix 1 of the Guidance. And that request should include a device description which describes the principles of operation of the device and any properties of it that are relevant to the clinical function.

Images and engineering schematics can also be included that help to illustrate either the principle of operation or how it functions clinically. Sponsors should include in their application package a proposed indication for use as well as a justification for how their device meets the designation criteria.

Finally, the sponsor should identify the planned marketing application in their submission. And I will mention if you would like more detail on what some of these elements are, they're included in Appendix 1 of The Guidance with more of an explanation.

This schematic summarizes the important review milestones that you can expect from FDA during our review of your Breakthrough Device Designation Request. We receive your request on Day 0 and begin our substantive review. We may send you a formal letter by Day 30 which identifies some deficiencies in your application, or you may receive interactive review questions or concerns from us regarding your submission.

Not all of our Designation Requests necessitate sending formal requests for additional information but some do. And it's not uncommon that we send these types of letters. If you do receive a formal additional information request letter it is important to note that this does not stop the review clock. So, if you have deficiencies to respond to, you need to respond by Day 45.

Our statutory deadline for rendering a final decision on the request is Day 60. And we'll communicate that decision to you with a formal letter. So, if a device is actually granted a Breakthrough Designation, as a sponsor you can utilize various programmatic options to obtain feedback on your device development through a special Q-Sub type that's called the Interaction for Designated Breakthrough Device Q-Sub.

We'll go over each of these options in more detail in the upcoming slides, but generally requests for feedback on breakthrough devices include review of the Data Development Plan, a request for what's called the Sprint Discussion, a request for a Clinical Protocol Agreement, as well as more traditional pre-submissions.

Additionally, FDA intends to offer sponsors of granted breakthrough devices regular status updates. And I'll provide some more information on what those entail in the upcoming slides.

So, the first type of feedback request which I mentioned was a Data Development Plan or a DDP. This is a high-level document which is intended to help ensure a predictable and transparent review of your device throughout the entire product lifecycle. It is an optional document and therefore it can address non-clinical evaluation of your device, clinical evaluation of your device, or both.

If as a sponsor you would like to propose any use of balancing pre- and post-market data requirements in DDP, it's important that you do so in order to initiate that conversation with FDA so that we have a good understanding of this proposal up front and can consider it in the overall regulatory path for your device.

Data Development Plans are often the first submission following a granted Breakthrough Device Designation that we work with a sponsor on. These submissions have a review timeframe of 45 days for us to provide you with our final formal feedback on the submission.

You will receive at the end of that 45 days either feedback or an agreement letter. And overall, we try to get to an agreement on DDP but it may take a

couple of iterations of the DDP and a couple of different submission supplements to get to that agreement.

We can also facilitate face to face meetings or teleconference as part of the DDP, but these aren't necessarily required.

The Program's Guidance Document does provide some example formats for DDP documents. Often, the non-clinical DDP is separate from the clinical study DDP.

And here on this slide I'm first showing an example for a non-clinical DDP. In this example, the type of non-clinical test or attribute is identified in Column 1. The relevant methodology and acceptance criteria for evaluating that attribute is described in Column 2. And the timeframe for when you expect to provide those results to FDA is described in Column 3.

So, I have a hypothetical example of a breakthrough device required some electromagnetic compatibility testing, that test would be identified in Column 1. And a proposed - the sponsor's proposed methodology for it would show up in Column 2. Here that would be the IEC 60601 Standard. And a sponsor may anticipate having those results available to support a feasibility study IDE.

As I mentioned, the DDP for clinical evaluation of a device is usually separate from the non-clinical DDP. And this here in the second table is an illustrative example for how the main study elements could be communicated in DDP format to the FDA for feedback. More information is available on the suggested content for DDPs in Appendix 2 of The Guidance.

The second type of interaction for designated breakthrough devices that I'll be talking about a Sprint Discussion. And this is a new type of request that's described in the Guidance Document. This is really a mechanism for sponsors who need very timely resolution of issues in order for their device development to progress.

We intend for them to be highly interactive with the ability for sponsors to provide additional information during the review period. Therefore, when you submit one of these requests, please be prepared to engage FDA and respond to our feedback's throughout the review period in order to facilitate the interactive nature of it and an ultimate goal of reaching mutual agreement on the path forward by the end of the review.

Due to the very interactive nature of these proposals and requests they're really most appropriate for a single topic with refined goals, for example, working out the details of a chronic animal study protocol.

Within The Guidance Document, we do provide an example timeline for a Spring Discussion and how the interaction between the sponsor and the FDA might be broken up over the course of that review period.

The Sprint Discussion ends with FDA sending a summary of our final feedback and the extent of agreement in the Sprint topic back to the sponsor.

The third option for feedback on a designated breakthrough device is a Clinical Protocol Agreement. The breakthrough provisions in the Food, Drug, and Cosmetic Act do outline a mechanism for sponsors to obtain written agreement on a clinical protocol with FDA. The extent of this agreement is considered binding on both FDA and the sponsor, and we document the terms and extent of agreement in a formal letter.

Finally, sponsors of designated breakthrough devices can also utilize other regulatory mechanisms for feedback. Some sponsors may want to submit a more traditional pre-submission with a larger expansion of topics in - as part of their breakthrough device development.

But we do request that you track - that you ask that it be tracked as an Interaction for Designated Breakthrough Device Q-Submission and that allows us to prioritize its review. Sponsors of breakthrough devices can also submit other types of Q-Submissions like Study List Determinations or Submission Issue Meetings.

It is also important to note that sponsors of breakthrough devices will get prioritized review for these Q-Submissions as well as the Investigationsl Device Exemption and Marketing Submissions that come in down the road.

So regular status updates -- these are not formal submissions -- but we do intend to offer a brief email or teleconference updates between the sponsor and the reviewer on the overall progress of their device development in between submissions.

These - in these discussions we do not advise for any data or feedback to be provided but we do recommend that sponsors and reviewers have one of these more touch base calls on about a bi-monthly basis as a way of keeping the lines of communication open.

Though the frequency of these interactions is largely based upon the needs of any current project the sponsor can initiate having these discussions with your lead reviewer after you've obtained a Breakthrough Device Designation and

hopefully set up a schedule to facilitate them and keep everyone up to date on the progress of the overall device.

So, in conclusion, the Breakthrough Devices Program is a voluntary one that's intended to expedite the development and review of certain medical devices for treating life-threatening or irreversibly debilitating diseases or conditions. There is a formal designation process where sponsors provide evidence or justifications for how their device meets the statutory criteria. The program provides sponsors with various mechanisms for engaging FDA early on in an effort to expedite the review and development of the device.

And overall Program success depends on commitment and engagement of both FDA and sponsors in order to facilitate the interactive and collaborative nature for the program. We do have an email box for questions regarding the Breakthrough Devices Program -- which is the Breakthrough Program email -- and on this page I'm highlighting some - a Web page as well as our final Program Guidance links.

Overall questions regarding The Program or today's presentation can be sent to the Breakthrough Device's Program's mailbox as well. Or for more general questions you can contact the Division of Industry and Consumer Education -- or DICE.

And with that I'd like to thank you for attending the Webinar and I'm happy to take any questions.

Coordinator: We will now begin the question and answer session. If you would like to ask a question, please press Star 1. Please unmute your phone and record your name clearly when prompted. Your name is required to introduce your question.

To withdraw your request press Star 2. One moment please for your first question.

Maureen Dreher: Thanks everybody. I wanted to just start out with maybe going over one question that we commonly get from stakeholders in The Program.

And that's to ask if the various Program options which are described in the Guidance Document -- being a DDP -- or a Clinical Protocol Agreement if those are required elements of the Breakthrough Devices Program and the overall regulatory path.

And the simple answer is that these are not required steps in the Breakthrough Devices Program once you've received a designation. These are really available options to a sponsor. And you can pick and choose from them depending upon what stage of development you're at in your device and what your priority is for obtaining FDA feedback on.

Irene Aihie: We'll take our first question.

Coordinator: Your first question comes from (Allison Komiyama). Your line is open.

(Allison Komiyama): Hi, can you hear me?

Maureen Dreher: Yep, we can hear you.

(Allison Komiyama): Hi, Maureen, thank you very much for taking my call and thank you very much for this Webinar. This is very helpful.

I'm a consultant. We have a lot of clients that, you know, come to us and say, "We have a breakthrough device." And I have a quick question about the first criterion. So, I know that it states that it's - the device is meant to provide some more effective treatment or a diagnosis of life-threatening or irreversibly debilitating human disease.

For - historically, and just based on - I know that once you give Breakthrough Designation to a company, it's up to them, you know, to - if they want to release that information or if they want to keep that to themselves.

Maureen Dreher: Yep.

(Allison Komiyama): For the ones that we have knowledge of, there have been devices that also prevent life-threatening infections and diseases. For example the (Therashield) endotracheal tube, the Polyganics liver sealant.

For those cases it sounds like FDA has also provided breakthrough status for companies that have a preventative device. So, it doesn't quite fall in line with the treatment or diagnosis. Is that still the case? Or has that, sort of shifted? And can you help define that?

Maureen Dreher: Sure, I can provide a little bit of clarity to that. I think it's an excellent question and I do appreciate you bringing that intricacy in the first criterion up.

The bottom line is if you have a device which you think may be breakthrough but it is operating in more of a preventative manner, it's worth reaching out to us really ahead of time to figure out if we would consider that to be eligible for The Program.

A lot of what we would do in making that call on if the device is somewhat preventative in nature is really to look very closely at how the device is being used and what its overall intention is.

So, it's hard to provide a more general answer but I think it is an intricacy of the criterion and something that's worth a conversation ahead of time with programmatic folks as well as the review team.

(Allison Komiyama): And then a follow-up question to that I guess: if we get, you know, an interactive request or a hold letter for additional information what's the best way to go about setting up a call with you or with the reviewer?

I guess there's some question about who is on the review team as well. Like, is it yourself, or who else is at..

Maureen Dreher: Yes, sure that's also a good question. So, let me take the second part of that first.

In terms of who makes up the review team there's obviously a lead reviewer and their management which is consistent with pretty much any FDA submission. That lead reviewer and management team will decide if certain consults are necessary.

I can tell you that many of our Breakthrough Device Designation Requests include a clinical consult and that weighs very heavily into the decision. People from The Program are not integrated into the daily review of each submission though we do discuss them, kind of at the - towards the end with the review team often.

And if the - we are here as, you know, an internal resource to address either the policy or interpretation questions with respect to the criteria. So, that's kind of the second piece of your question in terms of who would be on the review team. If you - I would like to use this as kind of, an opportunity also to clarify a little bit about the review process for designation requests.

As you noted, you may get - a sponsor an additional information request letter with some deficiencies in it part way through the review of a designation. Usually we send those out by Day 30 and sending that letter doesn't stop the review clock.

So, as a sponsor you have to respond pretty quickly -- within 45 days -- to that letter so that we can proceed with the review and meet our statutory deadline of 60 days for giving a final decision.

If you have questions about that - about any particular deficiency that comes, your best and most expedient course of action is to directly contact your lead reviewer. Like, call them up, send them an email, and say you would like to discuss the deficiencies, get clarity either on what they're asking for or what type of information is needed to address that concern.

(Allison Komiyama): That's very helpful, thank you so you much. I have 20 other questions but I will send them to the email address. So, thanks again for this Webinar, I really appreciate it.

Coordinator: Your next question comes from (Nancy Uch). Your line is open.

(Nancy Uch): Hello, can you hear me?

Maureen Dreher: Yep, I can hear you.

(Nancy Uch): Hi, thank you for the Webinar. I wanted to follow up on a slide that you had about the DDP as one of the tools available to sponsors.

And, you mentioned it's fairly high level but does incorporate our proposal to balance data collection in the pre-market and post-market setting. And then you also mentioned or described the protocol agreement as another tool.

Is it possible to incorporate or integrate those? Or is it - I guess my question is, is FDA flexible in looking at a protocol in addition to a DDP plan.

Maureen Dreher: Sure, so, any of the options which I utilized are available to sponsors of breakthrough devices at any time. And they can utilize multiple of those options.

So, you know, at the very basic level to your question yes you can submit a DDP request and separate request for clinical protocol - a formalized Clinical Protocol Agreement. Those are considered binding so they have, you know, pretty strict agreement letters that go out reflecting what the terms of that agreement are.

It's also appropriate within a DDP to talk at a bit more of a higher level about what the main elements of the study are. And to come to alignment on more of consensus on what the main elements of that study would be.

So, both of them are appropriate formats for getting our feedback on the overall clinical study and within a DDP we just tend to do it a bit of a higher level and it's not necessarily considered legally binding like the terms of a Clinical Protocol Agreement are.

(Nancy Uch): Thank you.

Coordinator: As a reminder, if you would like to ask a question, please press Star 1 and please record your name clearly when prompted.

Your next question comes from (Patty Bates). Your line is open.

(Patty Bates): Yes, hi Maureen. Thank you very much for the Webinar today. I have a question regarding the example in the appendix. At the very end of that example about the Planned Marketing Application there are three routes that we can use the PMA, the De Novo, or the 510(k).

So, my question is will FDA clearly answer in this pre - in the request if you've selected - if the sponsor has selected one of those as the planned route, will FDA clearly let you know if that is acceptable or if you needed to use a different route?

Maureen Dreher: Yes, that's an excellent question. And it's a point that - it's a question that we also often receive.

What that does is allow us to make sure that your planned marketing pathway is consistent with the options that are outlined in the statue. And it basically puts us on notice that we are expecting that type of marketing application from you.

But it's not - it's not, like, as formal as a 513(g) request where we're definitely saying that is the correct path for your particular device. And we don't have any language in our letters regarding that specifically.

(Patty Bates): Okay, so if you went - if you're submitting something requesting the De Novo route then we would need to submit a second pre-sub probably to get that confirmed with you.

Maureen Dreher: Yes, there's a separate process for confirming that your device would be regulated under a De Novo.

(Patty Bates): Mm-hm. Okay, all right great. That's all I needed. Thank you so much.

Maureen Dreher: Great.

Coordinator: Your next question comes from (Richard Cox). Your line is open.

(Richard Cox): Yes, quick question. Is the breakthrough mailbox operational during the shutdown?

Maureen Dreher: That is an excellent question and yes we are up - we are responding to inquiries at the breakthrough mailbox during the shutdown.

(Richard Cox): And so, also you will be accept - making breakthrough determinations during the shutdown?

Maureen Dreher: We are doing that.

(Richard Cox): Okay, thank you.

Irene Aihie: We'll take our next question.

Coordinator: Your next question comes from (Lubina). Your line is open.

(Lubina): Hi there, can you hear me okay?

Maureen Dreher: Yes, we can hear you fine.

(Lubina): Thank you, Maureen this is an excellent presentation.

I'm from (unintelligible) and I had a question for you -- a general question -- around whether or not ultimately for transparency and purposes of being able to help us make, you know, good thinking around whether something will qualify or not qualify.

Will there be some kind of database listing those products that have received Breakthrough Designation and a rationale? I know they do that on the Pharma side.

Maureen Dreher: Yes, I have seen that they do that in CDER for their program, however we do keep these submissions confidential and so we don't release the identity of devices which have been granted the designation publicly.

At times we will release the number of granted devices and talk about how many devices have been granted overall in comparison to how many requests we've had. But we don't - we consider the submissions to be confidential so we don't release the identity.

That being said, some sponsors do want to publicize on their own independently that they've received the designation. And so, they may do press releases or publicize that in some other manner.

(Lubina): Okay, thank you.

Coordinator: Your next question comes from (Trisha). Your line is open.

(Trisha): Hi, can you hear me?

Maureen Dreher: Yes, we can hear you.

(Trisha): Okay, thank you for the presentation. I had two questions, one of which were answered earlier.

So, the second question is more of a clarification. Regarding the Sprint Discussion I wasn't sure if it - was it a call? Or was that something that would be done through email or some written communication with the FDA?

Maureen Dreher: Sure, and that is a good question. There's a lot of flexibility in the overall Sprint format. The - I'm going to kind of start with the end of it and we'll back up a little bit.

But at the end of the Sprint Discussion we'll issue written formal feedback from the FDA that outlines the extent of what was agreed to and what the path is on the particular issues discussed.

And that will be formal. You'll get that in a formal manner. It's kind of the summary point of everything that was discussed during that Sprint.

But throughout the review period we did intend for them to be very interactive and for you to have the ability as a sponsor to submit new proposals or information during that review.

Often what we see is there'll be a couple of teleconference. Sometimes they have a face to face meeting included. But they are often teleconferences

throughout the Sprint period. And there may be two or three of them just depending upon what the issue is and how much needs to be discussed.

We do have an, kind of, example of how that review period is broken out in the Guidance Document. So, they're interactive throughout the review and then they end with a formal feedback being communicated to you that highlights and summarizes where everybody ended up at the end of that review.

(Trisha): Okay, thank you. Just a follow up to that - so, at the end of the discussion say there's a proposal that's made by the sponsor, is there a certain specific amount of time that the FDA takes to review that? Or is that flexible?

Maureen Dreher: So, maybe it would be helpful if I just gave you a bit of an example for what one set of interactions might look like in a Sprint.

Initially if a Sprint comes in the FDA review team and the sponsor should decide on and agree on the scope of what's discussed. So, we'll take, you know, ironing out the details of a chronic animal study as an example. And you're going to agree to work on that animal study protocol throughout the Sprint period.

We intend for these to basically be all wrapped up by about 45 days. There's a little bit of flexibility to that but that's the overall goal we have for these Sprint discussions. After the review team has a chance to dive into the protocol a bit they'll send you some initial feedback by email which you can provide alternate proposals to or - and/or additional information.

It's likely you'll have a call about that initial feedback maybe three weeks in, four weeks in to the review so you can, kind of, get more clarification on the

feedback, talk about some of your proposals for moving forward. Likely about a week or two later you would have a follow up call to discuss, kind of, where you - FDA's feedback on the alternate proposals or get to know information that was provided.

Then FDA would - in simple terms then FDA would send you our final formal feedback on that Sprint request and that kind of closes out the Sprint period. And hopefully by that time you've had a little bit of back and forth and had the opportunity to reach agreement on a path forward.

(Trisha): Got it, okay thank you that was really helpful.

Coordinator: Your next question comes from (Nina Augustus). Your line is open.

(Nina Augustus): Thank you very much; this was extremely useful and informative. Sometimes it's kind of a maze to walk through and you simplified it a lot for us. I had a couple of questions.

One question is, you know, most of the submissions that companies are expected to make almost always have to have a regulatory consultant onboard. Is that, kind of, expected with these, you know, one-on-one discussions with the FDA? Or is it something we can do without based on, you know, getting our criteria evaluated and we fit the guidelines of the DDP?

Maureen Dreher: So, it's totally up to a sponsor -- an individual sponsor -- whether or not they'd like to include a regulatory consultant as part of their submission process to FDA and the other interactions and discussions that you may be having with FDA.

We don't have any requirements on that on our side either way. It's totally up to a sponsor.

(Nina Augustus): So, there is a lot of one-on-one time with the FDA's lead reviewer and management team that might get assigned to each application?

Maureen Dreher: One of the hallmarks for The Program is that interactive and timely communication. And so, that - things like the Sprint Discussion and the DDP are ways that -- as well as the regular status updates in between submissions -- are ways that you get that interactive and timely communication that's one of the hallmarks for our program.

(Nina Augustus): Yes, that's great. And the other question I had is if you had multiple applications through the system that would get assigned based on whether it's diagnostic, therapeutic, and where we are in the development cycle, was that right?

((Crosstalk))

Maureen Dreher: I'm not sure I fully understand your question but I can give some clarity to how these designation requests come in. If the designation request gets sent into the DCC -- it's Document Control Center here at FDA -- it's assigned to the appropriate review organizational unit at CDRH based upon what the device is and its intended use.

So, if it's a diagnostic - clearly in vitro diagnostic device it's going to go to the relevant group in our Office of In Vitro Diagnostics and Radiological Health. Versus if it's a device that's intended to work during surgery it will go to our Division of Surgical Devices.

So, in that aspect we have designation requests that are parsed out to the relevant review organizational unit here at FDA on a regular basis.

(Nina Augustus): Okay, that helps. And just my last question. I'll be quick. .

If you have some devices that are already, kind of, mature in the process and have gotten regulatory approvals outside of the FDA, and they're currently in clinical use outside - I mean, that should not, you know, make it harder or easier for this application that we want to submit for a Breakthrough Device Designation?

Maureen Dreher: I assume by outside you mean outside of the United States? Is that correct?

(Nina Augustus): Yes.

Maureen Dreher: Okay, yes, if a device is marketed outside of the United States you can still come into us with a request for a Breakthrough Designation on that device. It - we would only need the Breakthrough Device Designation request prior to a Marketing Submission in the US.

(Nina Augustus): Okay, sounds great then. Thanks again, this was very useful and I appreciate your time and effort.

Maureen Dreher: Thanks.

Coordinator: As a reminder, if you would like to ask a question please press Star 1. Also, if you have multiple questions please limit your questions to one due to the volume of questions in queue.

Again, please press Star 1 if you'd like to ask a question. Your next question comes from (Kaneesha Jackson). Your line is open.

(Kaneesha Jackson): Hello, can you hear me?

Maureen Dreher: Yep.

(Kaneesha Jackson): Hi, so my question - and before I begin, again, thank you for the information. It's very helpful.

My question is in regard to companion diagnostics and really trying to understand if the corresponding drug or biologic has already received, sort of, the analogous Breakthrough Designation from CDER or CBER is that factored into CDRH's review of the companion diagnostic device?

And are there opportunities for, you know, sort of, any liaising between CDRH and CDER or CBER in review of these companion diagnostic devices?

Maureen Dreher: So, I can address one part of that question directly. When we have devices for either companion - designation requests for a device which is a companion diagnostic or if it's more - maybe a more traditional combination product, we do at times need CDER's input on that review.

And so that has certainly happened both for companion diagnostics and for combination products that - particularly if there's, like, a very novel aspect to that product. Regarding whether or not a Breakthrough Therapy Designation for the drug component of a companion diagnostic factors into our review, I think that's something that I haven't seen it directly.

So, it's probably best for you to go ahead and send that question to our mailbox and we can dig into it a little bit deeper with some of our colleagues in OIR who are more familiar with reviewing the companion diagnostics and the scope of what they've seen for designation requests.

(Kaneesha Jackson): Sure, thank you so much.

Coordinator: You next question comes from (Liam Mullen). Your line is open.

(Liam Mullen): Hello there, thanks for taking my question and for the Webinar.

I just wonder about Slide 23 where you talk about opportunities in terms of the balance of data collection for pre- and post-market studies and where scientifically appropriate.

And whether that -- and those principles in general -- apply just to the IDE Program or the 510 program - or the PMA Program or the 510(k) Program as well?

Maureen Dreher: Sure, good question. The statute actually says - and we've really been applying that primarily to PMA devices, not 510(k) devices.

We do have different post-market controls for PMA devices as compared to 510(k) devices and so, part of our assessment of whether or not it's scientifically appropriate goes into what data can be collected post-market. And it is something that we describe as being utilized on PMAs.

(Liam Mullen): Okay, and do you envisage any advantage in terms of all the data collection for 510(k)'s -- or their study designs -- versus devices that might not be considered for Breakthrough Designation?

Maureen Dreher: That's a pretty specific question that's going to get very much into the details of that particular device. So, in this type of format it's hard to comment on that. It may be something that we can have a conversation off-line about or may be able to address through an email to our Breakthrough Program mailbox.

But it's going to depend very specifically on what's being proposed and what the - both from the device side as well as from what you want to do in terms of data collection.

Coordinator: Your next question comes from (Frank Higgie). Your line is open.

(Frank Higgie): Thank you, very good seminar. I have a quick question. I wonder if you could elaborate on your earlier answer regarding prevention devices as qualifying under treatment under the statute.

Maureen Dreher: Yes, sure. There are - so, again it's very much going to depend on how the device is preventing - what the device is preventing and how it's performing that prevention.

And so, it is something that we'd want to discuss with the particular sponsor to get at before we can really say whether we think it would be eligible or not for the program.

(Frank Higgie): And that would come through interactions through your - through the Web site?

Maureen Dreher: Yes, if you can email the Breakthrough Devices Program mailbox we can initiate those discussions with you about a particular device.

(Frank Higgie): Thank you.

Coordinator: Your next question comes from (Sandy Williams). Your line is open.

(Sandy Williams): Hi, Maureen. Thank you so much for your presentation.

I have a question about Criterion 1 and specifically what - if there's some kind of minimum requirement or prioritization around mortality rates. So, if it's a life-threatening diagnostic device, you know, situation where mortality rate is perhaps low, is that prioritized lower versus another device where in those instances mortality rates are very high?

Maureen Dreher: It is a good question. We don't have a minimum bar for what you're referring to. As long as the device is subject to a PMA or a 510(k) or a De Novo then - and it addresses a life-threatening or irreversibly debilitating condition through treatment or diagnosis, then that's what we look at in terms of just the overall eligibility.

We would then dive into more of the specifics of how the device operates and what preliminary information is available to show that it meets Criterion 1. But we don't necessarily prioritize the review or the designation decisions based on mortality rate.

(Sandy Williams): Okay, thank you.

Coordinator: Your next question comes from (Steve Silverman). Your line is open.

(Steve Silverman): Thank you very much. I'm wondering if FDA is going to track and publish metrics regarding the program -- for example, metrics that reflect the

number of devices granted versus denied Breakthrough Designations, the percentage of submissions that receive designation, the total time to decision from designation, the number of subsequent interactions, et cetera?

Maureen Dreher: Yes, hi (Steve) thanks for that question. We are tracking a lot of that information internally. And right now it's being used to inform, like, some of the programmatic options and how we operate the program. It is good - it's really actually good to know that there's stakeholder interest in having that information available more publicly.

And so, I will take that back and - because we have to be a little bit careful about what the mechanism is that we would use to publish some of that information and making sure we can do so in a way that's de-identified and still protects the confidentiality of what we've received.

There's certainly, you know, some possibilities we could talk about there. And it is good to know that there is external support for that kind of idea.

(Steve Silverman): Thank you for your response. We understand the importance of de-identifying information and our membership is definitely interested in seeing metrics of the types that you discussed.

Maureen Dreher: Okay, thanks (Steve).

Coordinator: Your next question comes from (Pashwami). Your line is open.

(Pashwami): Hi, thank you for the presentation. And my question relates to the - one of the, you know, things about clinical data. As you mentioned that not a complete set of clinical data is required for designation.

It's also mentioned in the Guidance. So, my question is, what is - what's an example? Like, how many subjects do you look for? Any safety signal you look for? Or efficacy signal you look for? Or...

Maureen Dreher: Yes, sure.

(Pashwami): ...there any standard you applied to that data?

Maureen Dreher: Sure. So, what we're looking for is some information that there's reasonable expectation that the device is going to be more effective than what's available if there are alternative available or be effective if there's nothing else available.

And as you noted we don't expect for there to be definitive clinical data available at the time of designation. And some of our requests don't have any clinical data in them when we receive a designation. So, we're looking at their clinical data collected.

Certainly we're looking at it in terms of evaluation if theirs is showing a good potential for the device to operate as intended and to have a clinical impact. That's - we don't have a set, you know, criteria that we try to apply ahead of time to that because, you know, we're certainly going to see a variation in what we get coming in.

But we're looking to see, you know, certainly if there's credible - if the clinical data is credible and what potential it's showing on the technical success side and for clinical impact.

(Pashwami): Okay, great, thank you so much.

Coordinator: Your next question comes from (Lana Alexander). Your line is open.

(Lana Alexander): Hi, can you all hear me?

Maureen Dreher: Yes.

(Lana Alexander): I'm trying to make sure that this makes sense. So, you had mentioned that the Breakthrough Devices mailbox is open and still up and running during the shutdown. If device makers submit these requests as well as the - they have to also designate which pathway their device is supposed to take, correct?

Maureen Dreher: Mm-hm.

(Lana Alexander): And will that still take up to 60 days to be reviewed? Or has that been slowed due to the shutdown?

Maureen Dreher: No, it's a good question. We are operating that these Device Designation Requests will be reviewed in 60 days because that's a statutory requirement. So, that's the deadline that we have now.

(Lana Alexander): Thank you so much.

Coordinator: Your next question comes from (Alexander Hamed). Your line is open.

(Alexander Hamed): Hello.

Maureen Dreher: Hi.

(Alexander Hamed): I have a question on Sprint Discussion. There could be a scenario where the current Sprint the - the current topic is unresolvable at the time and maybe

more information is needed later in the product development. Is it allowed to move on and then reopen the previous Sprint?

Maureen Dreher: Yes, so, I'll clarify a couple of terms in my answer but the short answer is yes. You know, we do try to reach agreement on what the path forward is with the sponsor by the end of the Sprint period. And we anticipate that that should take about 45 days to do. But sometimes there are outstanding issues that aren't resolved as you've noted.

And our communication back to you at the end of that Sprint will - should clearly identify what the outstanding issues are that have not been resolved as well as what we've reached resolution and come to consensus on.

That closes out that formal submission period but you can always come back with an additional supplement which allows you to start talking about that particular topic with us again and hopefully get a bit further in coming to an agreement and a consensus with FDA on what the path forward is.

Sometimes the Sprint -- and this has happened -- sometimes it's better to close out a Sprint when you reach a point where you just need to think about it as a sponsor more in terms of taking what our feedback is forward. And, you know, coming up with some additional proposals.

And so, that's perfectly something we are able to accommodate.

(Alexander Hamed): Thank you very much.

Coordinator: Your next question comes from (Adam Collins). Your line is open. (Adam) please check your Mute button. Your line is open.

We'll go to the next question. It comes from (Kevin Yuraschevsky). Your line is open.

(Kevin Yuraschevsky): Hi, thank you very much for this presentation. It's always great to talk a real person at FDA rather than just going through the Web page.

My question deals with the parallel CMS approval process. Is there a way -- once you have Breakthrough Designation granted -- that you can link you Breakthrough Designation to some other accelerated parallel CMS approval opportunity?

Maureen Dreher: I certainly understand your desire to do that as a sponsor. Right now it is a separate process. And it's something that, you know - it's certainly outside the scope of our Guidance but I can tell you that they are separate.

(Kevin Yuraschevsky): Can you give me some direction on Guidance where I could find that?

Maureen Dreher: It's - I think that's something that you should address with CMS directly.

(Kevin Yuraschevsky): Thank you.

Coordinator: Your next question comes from (Lauren Clarke). Your line is open.

(Lauren Clarke): Hi, good afternoon. My question (unintelligible) is this age of product development that's expected before a BDD is submitted. Is there an expected level or stage of product development before submitting a request?

Maureen Dreher: No, there's not an expectation there. You're specifically - in particularly you're specifically asking about the DDP being submitted, is that correct?

Or were you asking about the designation request?

(Lauren Clarke): Yes, what would show a reasonable expectation of effectiveness and (unintelligible) tests with a device?

Maureen Dreher: Okay, sure so thank you for clarifying that.

We give one example of that in the Guidance Document. And we - it's just something that we commonly see in our applications as an approach for addressing that part of Criterion 1.

So, we're looking for evidence of both reasonable expectation for technical success and clinical impact. So, there we are - we commonly see some form of bench data which shows that the device can function as it's intended. So, it can do what it's overall been designed to do.

It's common for us to see that with some bench data. And then we might see some literature analyses or animal study data showing that the device - preliminary data from an animal study showing that the device would have a clinical impact.

With the literature analyses that we see, those are often related to the underlying principles of operation for the device and showing that they are likely to be more effective than what else is available.

Coordinator: As a reminder, if you would like to ask a question, please press Star 1 and record your name clearly when prompted. Again, only one question per caller due to the volume of questions.

Your next question comes from (David Chaddick). Your line is open.

(David Chaddick): Hi, Maureen. Very nice job. Can you hear me okay?

Maureen Dreher: Yes, I can hear you.

(David Chaddick): Good, so I have a question related to the timeline of this process and it appears that it's a 60-day review process. And you said that was statutory. I think it was out of 21st Century Cures.

And, the Guidance is 60 days and the Sprint paragraph says, "Within a set time period of about 45 days."

And earlier on in the question and answer period you replied to (Trisha) that we expect that when the Sprint comes in the sponsor, I think, would set up a schedule with the Agency about how best to resolve the issue. And that occurs in about 45 days.

And then initial feedback comes back to the sponsor and about two to three weeks later you anticipate the sponsor will come back to the Agency. We're at 60 already and we haven't...

Maureen Dreher: Sure, sure. Yes, (David) you're talking about a couple different processes there. So, let me give a little bit of clarity to a couple of different steps.

The designation request stage where FDA evaluates whether a device meets the criterion or not is one stage of the overall Breakthrough Devices Program. It's kind of the first step into The Program. And that review period takes 60 days.

You may get a deficiency letter from us about halfway through that 60 days. It doesn't stop the review clock. And at the end of that 60 days you're going to get a letter that says whether or not you have been granted Breakthrough Device Designation.

After a device and its use have been granted designation, then the sponsor could potentially enter into a Sprint Discussion with us if they wanted to in order to address a particular issue.

Within that Sprint Discussion -- that's a separate submission -- it's a different Q-Sub type, and that review period is about 45 days. We expect for teams to have a couple of conference calls with the sponsor during that review period and to send them their final feedback and the extent of what we've come to consensus on at the end of the 45 days.

(David Chaddick): And then, at the end of this final 45 days I submit my PMA, De Novo, 510(k)?

Maureen Dreher: That very much depends on where you are the development process and what that Sprint Discussion was about. You know, so, if you came in with a designation request that was just about to go to PMA then that might be feasible.

But many, many of our devices come in very, very early in their development. And so, it, you know, it still can be - they still need clinical studies before they even get to their PMA.

(David Chaddick): Yes, thank you. I would just fall back to (Steve Silverman)'s question about metrics and tracking and helping us understand timing. Anything de-identified would be very, very helpful, but thank you.

Maureen Dreher: Okay.

Coordinator: Your next question comes from (Mike Kuliak). Your line is open.

(Mike Kuliak): Yes, my question was answered previously by the dual - the question about a dual path with Breakthrough Device Designation and the parallel review. Thank you.

Coordinator: Your next question comes from (Julia Nelson). Your line is open.

(Julia Nelson): Hi, yes I had a question about a product that had a broad indication and if a subset of that indication could be used as a breakthrough device.

Is it possible to have a product declared a breakthrough device, you know, assuming there was clinical data to support the breakthrough portion of the indication and still have the initial PMA or 510(k) cover the broader indication with a priority review?

Maureen Dreher: Normally that's not how this program is intended to work. Within the designation request stage you also propose an intended use for the device, and that intended use has to meet the breakthrough criterion.

So, if there's only a subset of your proposed population that would meet the breakthrough criterion that's all that we could designate - that we could grant the designation for.

We do see broad indications come in in designation requests. And often we approach -- often, not always -- but often the approach that's taken is to try to understand from the sponsor if that's really the indication they want to pursue.

Or if they - or if there is a subset of patients that could be pursued as well and if that's something that they would like to do.

(Julia Nelson): So, if we were to get a breakthrough - an approval for the breakthrough device pathway for the subset indication but our PMA had the broader indication we would not receive the advantages? Is that right?

Maureen Dreher: Yes, we would be working with you through The Program on the subset of population that meets the breakthrough criterion.

(Julia Nelson): Thank you.

Coordinator: Your next question comes from (Marsha Yurost). Your line is open.

(Marsha Yurost): Yes, thank you. Like some of the other callers I am a consultant and in talking with my clients - oh, I'm so sorry about that phone in the background.

Severa; are quite excited about the provisions in The Program but have concerns about the implied and stated intensity of resources required of both FDA and sponsor.

So, the question that I have - is it fair to look at this as front loading of the regulatory effort in that more work earlier should ultimately streamline getting to a marketing designation?

What has concerned people about that interpretation is the statement in the Guidance that breakthrough devices might actually take longer. So, I'm wondering if you can comment on those issues.

Maureen Dreher: Sure, so that statement that you're referring to -- it's taken - it's come from our experience historically with the Priority Review Program where devices which have very novel scientific aspects to them - they're very complicated reviews.

And so, if you just listed their time in PMA then that might be longer than it is for other, more traditional devices that go through that marketing pathway. So, that's where that statement came from.

It is our overall intention for The Program to be interactive with the sponsor as much as we can and to give them an efficient path for device development so that the device becomes available to patients in a very timely manner. We are trying to view the whole development process in an expedited manner. –We doprioritize the submissions that come in for any breakthrough requests.

And the statement that you're referring to again is kind of - comes from the very novel scientific aspects of the device in our previous experience with the breakthrough - with the Priority Review Program. Under Breakthrough, you know, it is a new program.

We want to help sponsors get to the finish line in as expeditious a manner as possible whether that finish line is, you know, great success of the device and whether it represents the device not meeting its endpoints. You know, ultimately we're trying to figure out if the device is more effective and offers a great option for patients or if it's going to end up failing. And we want to be able to get there, to either of those places, in an efficient manner.

We want to continue to give resources in The Program to the devices which we believe will continue to meet the criteria and they are obviously showing promise as they progress through development.

(Marsha Yurost): Thank you, I think that addresses a great deal of the concerns. The other concern I've heard from some sponsors is what if -- at some point -- research constraints limit their ability to engage as intensively? Is there a no fault exit from the program? For lack of a better way to state it.

Maureen Dreher: If a sponsor decides after they've been granted designation that they'd like to withdraw from the program they do have the option to do that.

They can reach out to their lead reviewer to start facilitating that process or they can reach out to The Program mailbox. But that is an option if they decide at any time that they'd like to withdraw.

(Marsha Yurost): So, for example, if suddenly their resources become more limited they could do that at any time?

Maureen Dreher: Yes.

(Marsha Yurost): Thank you so much for that clarification.

Coordinator: And I am showing no further questions at this time.

Irene Aihie: Thank you, this is Irene Aihie here. We appreciate your participation and thoughtful questions. Today's presentation and transcript will be made available on the CDRH Learn Web page at www.FDA.gov/training/CDRHlearn by Friday, January 25.

If you have additional questions about today's presentation please use the contact information provided at the end of the slide presentation. As always, we appreciate your feedback.

Following the conclusion of today's live Webinar please complete a short 13-question survey about your FDA CDRH Webinar experience. The survey can be found at www.FDA.gov/CDRHWebinar immediately following the conclusion of today's Webinar.

Again, thank you for participating and this concludes today's Webinar.

Coordinator: Thank you for joining today's conference call. You may disconnect at this time.

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