FDA Webinar- Regulatory Overview for Developers and Sponsors of Neurological and Physical Medicine Devices: An Introduction to the De Novo Pathway
Moderator: Irene Aihie
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Operator: Welcome and thank you for standing by. At this time, all participants are in a listen-only mode until the question and answer session of today's call. At that time if you would like to ask a question, please press star 1. Today's conference is being recorded. If you have any objections you may disconnect at this time. I would now like to turn our meeting over to Ms. Irene Aihie. Thank you. You may begin

Irene Aihie: Thank you. Hello and welcome to today's FDA webinar. I am Irene Aihie of CDRH's Office of Communication and Education. As part of the FDA's ongoing efforts to ensure patients and providers have timely and continued access to safe, effective, and high-quality medical devices, today's webinar will provide developers and sponsors of neurological and physical medicine devices with information on the De Novo Pathway.

This webinar will provide an introduction to the FDA's role in facilitating innovations in neurological and physical medicine device technologies, an overview of the De Novo classification process, and information on working with the FDA and the presubmission process. Today Carlos Pena -- Director of

the Office of Neurological and Physical Medicine Devices in the Office of Product Evaluation and Quality here with CDRH -- will present an overview of the program.

He is joined by Sergio de del Castillo -- De Novo Program Lead -- and Patrick Antkowiak -- Team Leader of the Neuro Diagnostic Devices Team in the Office of Neurological and Physical Medicine Devices. Following the presentation, we will open the lines for your questions related to the information provided during today's presentation. Now, I give you Carlos.

Carlos Pena: Thank you, Irene, and welcome to all the attendees to our regulatory overview for developers, innovators, investigators, and sponsors of neurological and physical medicine devices. Our seminar today will primarily be focused on the De Novo Pathway and hopefully brings more safe and effective products to patients in the U.S.

Next slide. Today we're going to discuss the following -- instructions to review the neurological and physical medicine devices under the new medical program, the De Novo Pathway benefit analysis, case study, engaging with the FDA through the presubmission process, and a few closing remarks. Next slide.

My name is Carlos Pena and I'm the Director for the Office of Neuro and Physical Medicine and I am accompanied by two colleagues of mine -- Sergio and Patrick -- and you'll hear from them shortly about the De Novo program and the presubmission pathway.

So, next slide. Our office is one of several offices within the Office of Product Evaluation and Quality and the specific Office of Neurological and Physical Medicine Devices, speaks to the important commitment the agency (unintelligible) to this exciting, innovating, innovative, and emerging product (unintelligible). Next slide

At the FDA, the vision for the clinical devices and neurological Health is that patients in the United States have access to high-quality safe and effective

medical devices and public health importance first in the world (unintelligible) urgency and the De Novo Pathway is (unintelligible) to ensuring patients in the U.S. have access to this technology area.

Next slide. A medical device is defined as an instrument, apparatus, implement, machine or related article intended for use in diagnosis or cure, mitigation, treatments, or prevention of disease intended to affect the structure or function of the human body and does not achieve any of its primary intended purposes through chemical action.

And some of you are saying, "Carlos, there are several (unintelligible) addendums, clarifications. What is a medical device?" And if a diagnosis treatment will prevent the disease, it can be a medical device. It also does not achieve its intended use through chemical action, as noted. And importantly, one can classify a device as a medical even in the absence of (unintelligible) one of the (unintelligible) impacts or structural function of the human body. Next slide.

We have been engaged in this technology sector for some time and this is a favorite slide of the office. Here we show you an array of products with neurological indications (unintelligible) devices, (unintelligible) therapies, neurodiagnostic, (unintelligible), therapy devices for headaches, and multicatheters for the neuro (unintelligible).

Many of these products treat (unintelligible) a disease or condition. The goal is not to discuss the individual data and support of each device but share with here that each device goes through a regulatory pathway while is in part tailored to the individual (unintelligible) profile of the device, and including many times the De Novo Pathway. Next slide.

There are several pathways to market a medical device depending upon the specific device type and some discussion and focus on the De Novo Pathway, which is the second on the right-hand side blue arrow. And so you're probably saying to yourself again, "Carlos, there's a lot of pathways shown on the slide.

How do we find out what is needed for our product for the De Novo Pathway?"

And my response is that in this session, we're trying to focus not only on the De Novo Pathway -- which will provide additional details, a deep dive into this vision pathway -- but also on how best to engage through the presubmission process, which I've also said is a preprocess and folks should be okay to contact the agency to engage in this process of the presubmission aspect to get more information and more interaction with the agency to help hopefully move products to the marketplace. Next slide.

Medical devices are classified based on risk inherent, we present this through the classification Class I, II, and III. Class III is our highest risk (unintelligible) when we see several (unintelligible) each year (unintelligible) more invasive medical device technologies. Class II is our second highest risk classification.

We receive several thousand classification submissions in these (unintelligible). Class I is our lowest risk classification in development where they're typically (unintelligible) and generally (unintelligible) clarification. And so you might be saying, "Where is the De Novo?" And so this slide is the (unintelligible) De Novo submissions and I would like to turn to my colleague, Sergio, to take us to the next slide. Sergio?

Sergio de del Castillo: Thank you, Carlos, and welcome everyone. I'm Sergio de del Castillo. I currently serve as the De Novo Program Lead for the Center and I'm going to go over what exactly the De Novo classification Pathway is -- how it works, what kinds of products are meant for this Pathway, and then talk a little bit more about the review process from the FDA perspective. Next Slide, please.

So let me first by - first begin by explaining what exactly is a De Novo classification request. Next Slide. So, De Novo classification requests are specifically intended for new device types. What I mean by that is that there's something about that particular product that is fundamentally different from all existing neurological or physical medicine devices that are currently regulated and classified by the agency.

Because it's a new device type, it is automatically classified in the Class III, which means that normally it would require an approved PMA -- or pre-market application -- before it could be legally marketed in the United States.

However, alternatively, the De Novo Pathway provides another pathway to market. Instead, the manufacturer of the device can the new device type and request that the FDA classify it into Class I or Class II based on the probable risks to health for that product. Next slide.

Upon receipt of a De Novo request -- and I'll talk more about this during the review process section -- if we accept the file for review and it is in fact a new type of device, we will review all of the information that's been submitted in the De Novo and if we're able to classify the device into Class I or Class II, we will grant the De Novo request, which is essentially synonymous with approval or clearance.

Importantly in addition to giving authorization for marketing in the United States, we're going to create a brand new classification regulation that defines that new device type and from that point forward when we grant the De Novo, that type is regulated through the 510(k) Pathway and presuming that it is in fact classified as a Class II.

So, here is the connection with the 510(k) Pathway. After we've granted the De Novo, all other devices of that type -- whether they be new or modifications to that same kind of product -- are regulated through 510(k). Next slide, please.

So how do we know that your product is a new device type? You can advance one, please. There are three criteria that need to be met. The first is that it must meet the definition of a medical device and we think that this is relatively straightforward, but as we've experienced quite often in OHT5, sometimes there are products that kind of toe that line.

But generally speaking, most of the products we see meets the definition. The

next criterion, please, is that it can not fit into an existing classification regulation and this means two different things. First is that there is no predicate device. If you could advance one more, please. There's no predicate device. What this means is that your product -- in comparison to all existing classified products -- has no comparator.

If you were to try to submit a 510(k) for something that currently exists and try to claim substantial equivalence, you would say that you're not (unintelligible). There's something fundamentally different about your product but it doesn't fit into that existing regulation. Usually what this means is that your product has either a new intended use or different technological characteristics that raise different questions of thinking and effectiveness. Advance one more, please.

Also, within this criterion what it means is that your product cannot fit into an existing Class III classification regulation. If there exists a regulation that describes your device and it says that it is Class III and requires a PMA, then you have no choice. You must submit a PMA. You are not able to submit a De Novo classification request. One more advancement, please.

And then the final criterion is that it's not needing an approved PMA for that same device type. Many approved PMAs -- although Class III -- don't have an associated regulation with them.

However, this device type has been effectively determined a Class III PMA and because you or your product is the same device type, we would hold you to the same regulatory standard. So again, these are the three criteria that we're going to be looking at to determine whether or not your product is in fact eligible for De Novo classification. Next slide, please.

Once we've determined that your product is in fact eligible for De Novo classification and we begin the substance of review, the review team is going to be looking at these three classification goals. All three of these goals need to be met in order for us to grant the De Novo request.

This includes a determination that the probable benefits outweigh the risks to health, which is the Benefit-Risk Assessment. The next is that we need to be able to identify the probable risks to health of the device based on that Benefit-Risk Assessment and based on how the device is intended to be used. It's not how it may be used particular to off label use.

And then finally, we need to determine the level of control needed to mitigate those risks to health. If we can rely on general controls alone, we will classify the device into Class I. In most cases in De Novo land, we identify special controls in addition to the general controls to mitigate those risks, in which case we will classify the device into Class II. Next slide, please.

Depending upon classification goals, the FDA review team is going to attempt to create what we call our classification elements. These four elements are necessary for us to instill a grant decision and ultimately the final regulations.

That includes the Benefit-Risk Assessment, a risk mitigation table -- which summarizes the probable risks to health -- and the controls needed to mitigate those risks. If we determine that it is going to be a Class II device, we will also identify special controls needed to mitigate those risks to health, and then finally, we will create a new classification regulation itself. Next slide, please.

There will be a lot more discussion about this particular element later on, but I did want to highlight this at the very beginning because it's such an important element for a De Novo request and one of the most important aspects of the classification elements.

The Benefit-Risk Assessment is based on the totality of evidence presented in the De Novo but primarily is based off of the clinical data evidence that's presented. The assessment will include a separate assessment of the probable benefits and a separate assessment of probable risks and then those two are weighed against each other.

I highlight probable to point out that the benefits and risks that we identified

will be based on direct evidence through products, meaning that we have data to demonstrate definitively that this particular benefit or particular risk has some likelihood of occurring. We will not identify potential or quote-unquote theoretical benefits or risks as part of this assessment.

There will be a bunch of other factors that are considered as part of this assessment, some of which are listed here on this slide but it's (unintelligible) and there's more information about the Benefit-Risk Assessment in the guidance document, which is on another slide. And again, Carlos and others will be talking more about the Benefit-Risk Assessment later on in the presentation. Next slide, please.

Now I want to switch gears and explain a little bit about what you would need to think about when you're preparing a De Novo request if this the first time you're doing this. Next slide, please. Patrick Antkowiak is going to talk a little bit more about the presubmission process and how valuable and vital it is to the success of the De Novo review. I'm not going to talk about that at this point.

Instead, I'd like for you to focus on the resources that are listed here -- which I think are important background information -- so that you understand again how the De Novo classification works and also provides some of the expectations from the agency perspective about what we want to see in a De Novo request.

The first item that's listed here is our (unintelligible) device advice webpage for De Novos. This is sort of a one-stop-shop for all different kinds of publicly available information regarding the De Novo Pathway. I highly recommend that as sort of your first source of information as it has links to multiple pieces of information, such as guidance documents and publicly available databases.

And then the next two are just two many guidance documents that we've developed over the years specifically for the De Novo Pathway, but I think are probably the most important ones for you to read in the future. So the second bullet is what we call a De Novo program guidance.

Provides the complete overview of the entirety of the De Novo Pathway, including the legal foundations upon which they've left, as well as the review process and recommendations for content. And then the last item is our acceptance review guidance documents. You may have also heard of this known as the (R2) review guidance.

This explains the content that is required to be included in a De Novo request and the checklist that we will be using as part of our acceptance review to determine whether or not it can be submitted for a substantive review and further into the review process. So again, these are probably some of the more important resources for you to be aware of when thinking about De Novo classifications. Next slide, please.

Now I want to talk a little bit about the review process itself. Next slide, please. So in the (unintelligible), we have performance goals for De Novo for the first time and so based on those performance goals, our goal during the review of a De Novo is to try to reach a final decision by FDA Day 150. So this is the total time to decision for FDA.

Generally, the review is divided into two separate review cycles which we try to divide roughly equally in half, 75 days each. The first review cycle begins with the submission of the original De Novo. The team will look through all the data and information in that submission and it's not uncommon to have the team identify a number of questions or clarifications needed and even sometimes additional data.

While the team will try to get some of those things by interactive review, oftentimes what will happen is those questions will go into a formal request for additional information, which is a letter sent to the submitter and this puts the file on hold. The second review cycle typically begins when we receive responses from the submitter to that request for additional information.

We'll go through the remainder of the information that's been presented to us

and it is our intent to render a final decision in a second review cycle, and there are only two options -- to grant -- which is a positive decision -- or decline -- which is a negative decision. Next slide, please.

This is a very high-level process flowchart for the entirety of the De Novo review process. There are four major steps and we'll go through each of these in a little bit more detail. Next slide, please. Step one is the submission receipt. So this is the submission of the original De Novo request to our Document Control Center or DCC.

At this stage, the DCC is only verifying two things -- that one, we've obtained the applicable user fee; and two, that you provided a valid electronic copy or eCopy of the De Novo submission. If those two criteria are met, the De Novo is entered into our tracking system and it is assigned to the reviewer to begin the next step of the review process. Next slide, please.

And the next step is the acceptance or (R2) review. As I mentioned, this is intended to look through the submission to determine if it provided all the necessary content (unintelligible) is considered administratively complete in order to proceed to the substantive review.

At this stage, we're trying to complete the acceptance or (R2) review within 15 calendar days from receiving the original De Novo request. Once it's been accepted for review, you will proceed to the next step, which is a substantive review. Again, there's more information about this stage of the review process in the guidance document listed at the bottom of the slide. Next slide.

Next is the substantive review. Again, we've accepted the De Novo based on whether or not the content that's prior to (unintelligible) has been presented. The first thing that we're going to do is (unintelligible) and verify that the device is eligible for De Novo classification. That is making sure that it is a new device type. If it is eligible -- meaning that it meets those three criteria I mentioned earlier -- the team will then proceed and to review all the information and data the De Novo.

This will include a Benefit-Risk Assessment based on the available information. Again, we will identify any questions, what we call deficiencies, and where feasible, we will try to have those questions answered through interactive review, which does not stop the review clock. Next slide, please.

However in most cases -- not always -- but in most cases, we'll often identify quite a number of questions for the submitter -- most of which cannot be resolved through interactive review -- in which case we'll put all of those questions and deficiencies into a formal request for additional information letter, which stops the review clock.

From the moment that we send that AI letter, the submitter of the De Novoa has 180 days to provide complete responses to each of the deficiencies that are identified in that letter, which is a critical piece of information. Next slide, please.

Then the final step is the final reviewing decision and generally, this starts once the submitter has provided responses to that request for additional information letter. We'll first determine whether or not complete responses have been provided to that letter. If not, then it goes back on hold until we receive all the requested information.

If it is complete response, the review clock starts again and we'll proceed with reviewing all the responses, including any new data that has been submitted. As part of that review during this final step, we will update our Benefit-Risk Assessment based on any new information or data that's been given to us as part of that response. And again, it is our intent to render a final decision at this last step of the process. Again, there are only two options -- grant or decline. Next slide, please.

And I just want to briefly explain the two decisions that are possible for us to make. For a declining decision, the typical reasons why we decline a De Novo are generally going to be based off of the Benefit-Risk Assessment, which

again, we'll talk about more in just a moment.

Another common reason we decline a De Novo is that we're not able to develop to determine a special control to mitigate the probable risks to health, and what this usually means that there's some sort of issue with the non-clinical or bench information that's been presented to us.

Either there's something that's missing that we think is required or -- although it's been submitted -- there may be some issues with the testing that's been provided to us in terms of the test methodology or the results. And then -- not commonly -- we can also decline a De Novo if in fact, we determine it's not eligible for De Novo classification.

What this usually means is that we do think that there's a reasonable predicate device that could be used and therefore, the device can be regulated through 510(k). If we decline the De Novo, we will issue a letter or order the requester that will identify the reasons for the decline decision and all the outstanding deficiencies that we think need to be addressed in order for us to eventually grant the De Novo request. Next slide, please.

Hopefully, however, we are moving towards making a decision. Again, there are three classification goals that need to be met in order for us to grant the De Novo. Again, probably benefits outweigh probable risks, identification of a probable risk to health when the device is used as intended, and then a determination of the controls needed to mitigate those risks. General (unintelligible) controls that loan to mitigate risks means that it will be classified as a Class I. General and special controls needed to mitigate risk means it'll be classified into Class II. Next slide, please.

I also want to explain procedurally what happens after a De Novo is met because there are actually quite a few activities that occur. Once you send the ranking order -- meaning that your De Novo has been granted by the agency -- at that point, that device is considered legally marketed in the United States, subject to any of the requirements or medications that are in that ranking order,

including the special controls that have been identified if it's Class II.

Also at that moment, we will create the new classification regulation and is considered established and in effect as soon as we turn that ranking order to the submitter. Also at that point, the De Novo device that has just been granted can be used as a type of device for future 510(k) submissions. Next slide, please.

We will also provide some publicly available information in our publicly available De Novo database, which is linked here in the slide. We will include the granting order that has been submitted to the submitter of the De Novo unredacted. It will also include what's called a decision summary.

This is very similar in concept to a 510(k) summary (unintelligible) or a PMA (unintelligible). It's a summary of all the data and information that we used from the De Novo to come to our granting decision. It's an excellent source of information to understand the kinds of information and data that the agency uses to be able to classify any device type and so I encourage you to look through the De Novo database on your own time to look through that.

Also, you're required by law to publish a notice in the Federal Register announcing the new classification regulations that we've created and this is the mechanism by which we update the code of federal regulations to include that new classification regulation. Next slide, please.

So, in summary, the De Novo classification Pathway is intended specifically for new device types and again, what this means is it's for a device that is fundamentally different from all other neurological and physical medicine devices that we currently classify and regulate.

If it is eligible for De Novo and we accept it for review and we grant it, not only can you legally market your product in the U.S., but we're going to create a new classification regulation that defines that new device type.

The classification decision that we make will largely be determined by the

overall Benefit-Risk Assessment and the controls that are going to be needed to mitigate the probable risk to health of the device. And now I'll turn it back over to Carlos. He's going to talk more about the risk assessment.

Carlos Pena: Thank you, Sergio. Next slide. As Sergio mentioned, the classification for determining part by the Benefit-Risk Assessment, I would like to turn to discuss our benefit-risk determination (unintelligible). Next slide. Benefit-risk determinations can include the following -- (unintelligible) considerations of probable benefits and probable risks.

As part of this determination (unintelligible) of taking (unintelligible) for the device (unintelligible) use both chemical or non-chemical (unintelligible) in benefit-risk determinations, and probable risks and probable benefits should be supported by valid scientific evidence. Next Slide.

As part of the determination is identifying a reasonable assurance of safety, which occurs and it can be determined based upon valid scientific evidence that the probable benefits outweigh any probable risks and can be demonstrated by establishing the absence of unreasonable (unintelligible) for injury, such as the use of the device for its intended uses and conditions of use.

Next slide. Benefit-risk determination is also (unintelligible) assurance of effectiveness of a device that shall consist principally of (unintelligible) controls investigations as defined in the (CFR), unless the commission authorizes reliance upon other valid scientific evidence which the commission has determined is sufficient evidence from which to determine the effectiveness of the device, even in the absence of controlled investigations.

The commission will make such a determination whether the requirement of well-controlled investigations is not (unintelligible) device. So there is some flexibility in tailoring (unintelligible) device, keeping in mind well-controlled investigations are principally accepted. Next slide.

Importantly, there are several factors that FDA considers in the benefit-risk

determination. For example, benefits can be further described with regards to type of benefits, the magnitude of benefits, the probability the patient experienced one or more benefits, the duration of the effects of those benefits, and the degree of uncertainty of the benefits.

And similarly, the risks can be further described with regard to (unintelligible) types and number and rates of harmful events associated with use of the device, the probability of a harmful event, the duration of these events, and the risks from false positive or false negative results, the diagnostic in particular and the degree of uncertainty. So these are the different factors that are involved in FDA's review - next slide.

Furthermore, even the fact that in the previous slides can be further (unintelligible) by the type of benefit evaluated or the magnitude of the (treatment) effect all the way to the duration of the effects and how it was determined because in the bottom row is the duration of benefits achieved the value of the patients. So these are the types of considerations that sponsors should be well informed to present and share with FDA - next slide.

Another name for risk and prevention is the type of adverse events (unintelligible) to the extent of the patient population duration of events to name a few are further considerations to evaluate during the benefit-risk assessments - similar to benefit considerations - next slide.

And there are also additional factors that should be part of the dialogue between a sponsor (names) seeking certainty around these benefits from this -- patient-centric assessments and patient (unintelligible) outcomes, characterization of the views, patient's perspectives overall, the availability of alternative treatments for diagnostics, risk mitigation, post-market data, and the novel technology investment in unmet medical need -- which will all be (unintelligible) to that assessment - next slide.

So if you take a look at a hypothetical case study, let's throw their game in during a potentially innovative, low-risk device to the market place - next slide.

Let's say we have a device called the (unintelligible) two payment(unintelligible) particularly with (unintelligible) off and on instructing them. Our first step is in the final technology and its intended to use. The technology to (unintelligible) battery-powered device with low energy electric pulses controlled by a mobile app that requires perhaps 45 minutes for (unintelligible) and then turns off automatically - next slide.

Step 2 would then be to determine whether the products or the medical device and in this case, it is intended to treat a disease in humans or a condition in humans - next slide.

In this process, we would then be focused on determining that this device is eligible to deliver classifications. And the two questions just list that (unintelligible) had reviewed for us is that if their product was Class 2 or Class 1 status or is there a similar Class 2 to an A device or is now a technology (device) - next slide.

And I think that the further questions to ask whether to is there a (unintelligible) marketed similar device? The (unintelligible) device had the intended use of the market's similar device? Does the (unintelligible) have the same technological characteristics of a marketed device, and do the different technological characteristics raise different sessions of statements in the marketed device? And these are all the questions that would be folded in along with the (unintelligible) - next slide.

And one particular question is, is there a saying in terms of use? And the answer is no. These questions appear, you would then move to Step 4 - next slide. And Step 4 would involve assessing the risks and litigation to the device (unintelligible) and (unintelligible) to general controls or general and special controls provide these (unintelligible) have (unintelligible) effective - next slide.

If so, the Step 5 would usually (unintelligible) with FDA and check then.

Typically FDA's responses on the steps to either (unintelligible) questions, (unintelligible) information medical device, or in some cases a presubmission which can have questions that is the first four steps reviewed in the prior slides. And (Patrick) is going to talk a little bit more about this in his presentation.

And fortunate that (neither) of these submissions represent final FDA decisions with regard to legally marketing a medical device in that case and that would require the actual level of (commission) - next slide.

If we move ahead, Step 6 involves FDA engagement and the types of steps we will be performing including a classification review of the device, a benefit-risk review of the product, and (unintelligible) review of physical (unintelligible) of device technology, (fire) safe and additional evidence related in support of the device according to our (picture) - next slide.

So that in Step 7 we can make a fully informed benefit-risk assessment about the device which will be important for the legal market of a medical device in the US. And I should mention, these steps involve a number of interactions which can best (unintelligible) within the presubmission pathway which (Patrick) will walk us through in the next few slides - Next (Patrick).

(Patrick Cancovia): Thank you (Carlos). Hey, I'm (Patrick Cancovia). I'm the Team Lead for the Neurodiagnostic Devices Team and I'll be discussing some best practices for preparing a few submission for your De Novo application - next slide, please.

Much of the information that I will be discussing is described in the Presubmission Program Guidance documents which is accessible at the link on the slide. And while that guidance covers multiple types of interactions, I'll just be focusing on the presubmission. Presubmission represents an opportunity to interact with FDA and obtain feedback on many aspects of your device.

And it will be likely most relevant for you prior to submitting your Business De Novo Marketing Application. And the feedback that we provided free has no associated user fee and it is confidential. We won't be publicly disclosing this.

And since pre-submissions have submission numbers that always begin with the letter Q, you'll also see them referred to in this webinar presentation as Q (subs) as well - next slide, please.

For the presubmission guidance outline the timeframe for review, if you request to hold a meeting with (unintelligible) have that meeting within 35 to 90 calendar days of the acknowledged fee for your submissions, we'll aim to provide you with written feedback around five days in advanced of your scheduled meeting days.

And after you receive (unintelligible) feedback, if you have no further questions on the feedback that you need clarification on, you're certainly welcome to cancel this meeting. And as mentioned, typically we won't be able to have a meeting earlier than that 75-day timeframe due to workload considerations for our (unintelligible) staff.

Lastly, we urge you to budget the meeting time accordingly for a one-hour meeting and for generally not able to hold meetings longer than an hour per presubmission feedback clarification - next slide, please.

So as Dr. (Penny) noted, you can engage with us in a presubmission while the device is still in the early stages of development. Early FDA engagement with the presubmission presents a chance to identify potential issues and address them appropriately. And this can be particularly helpful if you have a very novel device technology or if you'll need substantial testing or clinical data to support your devices' performance claims.

And after you've received feedback in an initial presubmission, you are always welcome to submit the supplement at a later stage in the device's development if you'd like additional feedback based on some changes that you find to adopt the feedback that we've given - next slide, please.

One common issue that sponsors frequently have with pre-submissions is having them in a correct eCopy format. In order for a presubmission to be

logged in and reviewed, the submission will have to comply with the eCopy guidance linked on the slide.

And if you don't comply with the eCopy guidance, the submission will not be logged in and will not be reviewed until we receive a valid eCopy. If you have any questions about the eCopy format, we prefer to be emailed to us linked on this slide - next slide, please.

So what should your presubmission contain? At a minimum, you'll need a Cover Letter, background information on your device. That includes the device description, intended use, (plants) and animal testing protocols, and clinical protocols.

We'll often need to provide specific questions for FDA to address and we'll have a little bit more on those in a bit. Please note that you should not include data in your presubmission such as data in your clinical study that you have conducted. It is our policy not to review data provided in a presubmission - next slide, please.

And for a presubmission related to a future De Novo, latest we recommend removing some of the information that (Carlos) and (Sergio) described in this webinar including a proposed device class -- either a Class 1 or Class 2 -- a discussion of some of the relevant existing device classification regulations and why you believe your device would not fall into those benefit risks analysis and propose special controls that mitigate those risks if you believe that your device would fall into Class 2, along with any prior regulatory history that you've had - next slide, please.

Another common issue that we see often is that the submission does not include enough information upfront for us to review. So while we do recommend that you engage us early in your device development process, we believe that -- at a minimum -- (and show) that this has identified your devices' intended use and some key-defined aspects before sending us a presubmission.

So please be mindful that a lack of upfront device subscription information effective for devices that are really novel technology or that we don't have a lot of history with might hinder the chances for us to have a meaningful discussion - next slide, please.

And if the commission doesn't include enough information upfront for us to understand how your device works and how you intend it to be used, what will happen is that we'll end up reaching out and asking a lot of clarification questions that will take time for you to provide some complete answers to and this ends up extending the overall length of the review - next slide, please.

So the things to be mindful of is the fact, you know, remember that you are the expert on your device and you know the most about its technology. The more that you can explain your technology and your rationale for how you developed it or plan to develop it, the better. And then we'll be able to focus all of our efforts on giving you better feedback - next slide, please.

So when it comes to providing background information, our general rule of thumb is that more is better at least as long as it's (level) organized. In our experiences, it's better to air on the side of providing more information than you think that we would need. If you're citing literature articles to support the device parameters or clinical study design, we requested that you include English copies of those in your presubmission.

So now with all that being said, it certainly is a thing but the thing that's providing us with too much information. If you're sending us things like details surface diagram, you know, thousands of lines of software code or a copy of the grants that was used to support your device, that's probably more information than we need to understand your device to answer and address your presubmission questions - next slide, please.

So we also recommend that you avoid making assumptions about (unintelligible) and providing background information. Unless there is an applicable guidance, standard, or other regulatory precedents, we recommend

that you identify the most appropriate approach for your needs and provide a justification for that. For example, suppose you are planning to support the right to safety with an animal study.

Well, not every animal study needs to be a non-human primates model. You know, other models or approaches might be more acceptable provided that (unintelligible) provide information that testifies that other models -- along with a protocol -- that meets your particular situation - next slide, please.

In your submission, you should be asking us specific questions which we will provide feedback. The most common issue that we see with these specific questions is that you haven't provided your own proposal for us to review. For example, we wouldn't be able to provide, you know, answers to questions like, what type of animal model should be used or what should our clinical control group be?

We think that those are your responsibility to determine as long as you're providing justifications for it. And as we noted earlier, we also wouldn't be able to answer questions about the review of data. (unintelligible) FDA have any comments on benign clinical test results we've provided - slide, please.

So generally, the best type of specific questions that we see build on background information you provided and include a proposal for us to review. So for example, if you're providing an animal model with a rationale in your submission, a good, specific question would be what concerns would FDA have about the proposed animal model to support the device's safety?

We'd be very happy to give you feedback on a question like that. And similarly, if you're describing a clinical control group, a question that we could give feedback on is, you know, based on the intended use, we selected the clinical control group in our proposed study appropriate - next slide, please.

And lastly, here are a couple of specific questions that might be useful for De Novo device submission that we could answer, and these questions are broadly

applicable to a variety of device types. Like questions like, based on the information provided that include device description and intended use analysis of (products).

So does FDA agree that my device is eligible for a De Novo submission? Or, does (unintelligible) believe that there are risks other than the ones that we've identified that must be mitigated or are there other special controls that should be considered to provide a reasonable assurance based on the effectiveness?

In summary again, I'd like to recommend that you engage in the FDA and the presubmission as early as is practical for you. I'll now turn it back over to Dr. (Carlos Piinya) for some closing remarks.

(Carlos Pinya): Thank you (Patrick) - so for a few closing remarks and attention so far in the session. One is (choosing) the slide in our De Novo pathway if you believe you're (unintelligible) is appropriate for this path. The slides provide a lot of useful information that can help eliminate this process including a few slides at the end that have links to related guidance and topics that we've discussed today.

Two, if you think it's too early to contact FDA, that's the best time to contact FDA. And we urge you to review the presubmission pathway along the way which is a free process. Direct engagements with FDA with claims to the most valuable and critical way in which we can both match expectations for the product you are interested in (unintelligible) the market to the benefit of patients and their families.

And three, if you still have questions, we urge you to begin to contact with us with our Division of Industrial and Consumer Education. And that is a good starting point for further information about the De Novo pathway. We're also readily available to help all sponsors and innovators and investigators in this technology area and submission pathway and we look forward to future interaction. I think you'll be surprised with the engagement that we get from FDA. So then this slide will conclude to the presentation part of our session -

(unintelligible).

Woman 1: Thank you, our operator will now take questions.

Operator: Thank you - if you would like to ask a question over the phone, please press star 1 and record your first and last name. To withdraw your question, you may press Star 2. Once again, to ask a question, please press star 1 and record your first and last name.

Thank you - just a few moments for questions.

(Carlos Pinya): While we wait to see if there are any questions, a couple of questions that might come to mind to folks is just how much information can you provide FDA about the benefits of your device? And our answer is please provide as much information with regard to the information as it relates to a device including benefits and risks. That information will help (process) our review and work with you in bringing that product to the market.

A second question is, you know, what if I have specific questions about my own device, specific technology questions or submissions pathway questions? And I would say, you know, again to start off at the division of industry and consumer education, they can field several types of questions.

And if they believe that the hedge of questions that you all may have maybe a little bit more detailed for our Office of (unintelligible) of Physical Medicine, they'll direct us - they'll direct sponsors to our office as appropriate. But there is a variety of (quotas) in the agency I think sponsors and developers and innovators can engage with the FDA as needed. Let me stop there.

Woman 1: Thank you (Carlos) - Operator, we'll pick up for questions.

Operator: All right our first question is from (Allison Kamiyama). Your line is open.

(Allison Kamiyama): Hi, thanks so much - awkward going first. First is for this webinar,. This is

extremely helpful. My question is historically a moderate-risk device might have been designated as a Class 3 PMA device due to the De Novo process being not as well defined or as frequently used as it is today.

And it is my understanding that it is up to the manufacturer that they will pursue the PMA or De Novo Pathway for their device if there is no true predicate. With that in mind, some companies may use or may have used the PMA pathway as a barrier to market for other manufacturers as future similar devices will also need to submit a PMA to get market approval.

The reclassification process after a regulation is generated is challenging and can take many years. Therefore, does FDA have any mechanism or considerations on how to reduce burden from moderate-risk devices that due to historical reasons now require a PMA? I believe this is in line with FDA's mission to promote public health through technological advancement - thank you.

(Carlos Pinya): Sure I can start us off (Allison). I'm glad you're on the phone. It's good to connect during the (unintelligible) time. So I would recommend that for a specific discussion. I think we're clicking on (unintelligible) and tailor the response to the individual sponsor and their technology. I think that's where a lot of clarification can happen.

And the way to do that is going to be via our presubmission pathway. There may be nuances with one pathway over the other, but I think the details about how to address moving a product to marketing in the least burdensome way would best be addressed via the presubmission pathway. That would be a good first step. That could be a quick clarification to focusing which submission pathway is best for the sponsor - thank you for that (Allison).

(Allison Kamiyama): Yes, thank you.

Operator: Thank you - our next question is from (Eric Chen). Your line is open.

(Eric Chen): Thank you for that and thank you (Carlos) and FDA for, you know, having the opportunity to present us on this issue. And I think it's very, very helpful for the community. I had a general question and perhaps you may not know the (data) for this. But I'd be curious for the (unintelligible) that your office has seen, could you perhaps give an idea of the amount of the De Novos that require some type of clinical data to support benefit-risk of the device?

(Carlos Pinya): Yes, (Patrick), do you want to take this one or do you want me to start?

(Patrick Cancovia): Why don't you start (Carlos) and then I can chime in if needed.

(Carlos Pinya): So that's a great question (Eric). I think, you know, I think when we look at the De Novos, it is general. They're involved in some type of (political) information about the benefits to patients. And so it would be not - It would be unusual not to say it's rare but there would be some - there should be and there could be some information about clinical information about the product that would be needed for the review on looking at the benefit for that product.

And so, you know, I'm going to say a really defined word is that for a particular submission, clinical data may be needed and it really depends upon what the device does, the prior studies, the technology used, the previous information you have, U.S. overseas information, and these types of - this type of information is probably going to be best evaluated in the submission.

And again, you know, I think if we're going to become a routine response perhaps but the presubmission factor would be a really good opportunity to identify what clinical evidence may be needed for any particular device because that's going to be like I mentioned in the introductory slides. Our reviews are really tailored to these standard benefits and the subjects of the product which may involve clinical data. But that's a good question (Eric). (Patrick), did you want to add anything?

(Patric Cancovia): Yes, I think in addition to the presubmission pathways to talk about what could be the potential, you know, looking forward prospectively what type of data

you would need, that would be the way to those with best (unintelligible).

But if you're interested in getting a historical understanding of what types of data is needed to support what types of products with, you know, intended uses and certain benefit-risk evaluations are likely available De novo summary database, you know. It discloses all of that information so you can at least get a sense of what has been provided to support -- what Facebook product -- in their public database.

(Eric Chen): Okay great - thanks for that.

Operator: Thank you - our next question is from (Courtney Williamson), your line is open.

(Courtney Williamson): Great, thank you so much for the presentation. I have a question about software as devices, so particularly looking at wearable devices and those devices having substantial software components. Could you talk a little bit about how the De Novo pathway interacts with those types of devices?

(Patrick Cancovia): Sorry, yes, thanks (Courtney) - yes (Carlos), I can start with this one and maybe you can jump in. Yes, software as a medical device can be, you know, that certainly is a pretty hot area and you can again look at the De Novo databases and get a sense of what's been done there.

You know, we evaluated (unintelligible), you know, as the same as we evaluate De Novo in general. We're looking for safety and effectiveness and whether the benefits outweigh the risks

You know, so while there are some unique aspects to (unintelligible), we're still -- in general -- looking at the overall big picture at the same type of data and requirements that we have for a device that's not a (unintelligible). There can be some interesting regulatory aspects about (unintelligible) that, you know, again and not to believe there's a presubmission process.

Again I'm going to (waiver) it. That's a great way to talk about some unique aspects that (MT) does bring up. But, you know, in general -- (unintelligible) the device -- it still needs to show the same level, you know, of benefits for the intended uses that non (unintelligible) would as a say in general. And I don't know if you have any thoughts to add on top of that (Carlos)?

(Carlos Pinya): Yes, I mean I think from the questions that we're getting, you know, one sort of common thread is the evidence, the, you know, the clinical evidence, what's the clinical evidence? How much, you know, what is unique about the software and medical device area.

And (Patrick), I think you started - you made additional comments that really was a good one is that, you know, despite the unique characteristics of one device type over another, the benefit/risk analysis, the calculus, is really key. I think slides 39 to 40, which talked about both the benefit considerations and the risk considerations. This is quantifying the type of benefits, the management of benefits, the duration of effects.

I would like to encourage the sponsors and developers to talk about both the benefits and the risks which leads back to, you know, tailoring our review of what you've provided about your product and the risk and the severity of risk probability of a harmful event duration.

The benefit/risk calculus is - you spent intentionally several slides during the presentation to talk about these issues. And I think that would really be helpful going forward in the De Novo program, especially in the neurological and physical medicine devices, is if you can help us understand - and this is directed to the sponsors and investigators and the developers and innovators.

Help us understand the benefit/risk assessment and why your product - the benefit for your product outweighs the risks. That would be - I think if we're all on the same page, if we can all crystallize that discussion and if we can agree on that discussion we'd be in really good shape.

But you know, depending upon - I know the device types can differ from one to the next. But the benefit/risk calculus that (Patrick) and I and (Sergio) have spent some time on, it's like a key step for us that we could use your help in making sure we understand the most about your device that you're the experts of. Hopefully, that's helpful.

Woman: Yes, very much, thank you.

Operator: Thank you. Our next question is from (Matt Trabella). Your line is open.

(Matt Trabella): Thank you very much. Very good presentation. And you guys did cover quite a bit of related to assessing whether the new technical features of the device might push it into De Novo versus 510(k) world. I was wondering if you could maybe talk about - you know we're very much in that gray line area.

We have something that potentially has some new features and we're deciding whether to scale those back and try to be more like the predicate devices in order to get (unintelligible) acceptance and then perhaps to get De Novo down the road to get the fully capable device to market.

Or you know maybe leading with a De Novo device first. And I'm wondering if you could maybe talk about the time to market differences between those two approaches and you know, maybe some pros and cons of each?

(Carlos): Yeah, (Patrick) let me start with this one. I - so, and all these questions that we're getting are really good. So I think in looking at what regulatory pathway may be appropriate for your product, I think what I'm hearing though is that there is an opportunity for you to modify or refine your product based upon what it may be similar to or how it may be different based upon those changes.

And what I think would FDA could best be with helpful is identifying the pros and cons for what you choose. We'd be giving you information about the options that you have with regard to regulatory choices for your products. So we would be deferring to you on the business decisions you make about that

product.

So while there may be advantages with you know, one regulatory pathway over another, I think it would be important for you - for us to have a more focused discussion on what those changes that you might be thinking about with your products and hearing from us the regulatory options table that we could sort of walk you through.

And I say regulatory options table informally. You know, the regulatory options that would result based upon the changes, one change from the next. And that could best be - you could best have a discussion in the pre-submission. But you know, that's a great question. Many times folks come to us and say, you know, what does FDA think?

And I think FDA's role is to provide regulatory options for you to make your best business decisions because the business decisions you make, you know they also impact economics and other considerations. But you know, how we can best be helpful is providing regulatory options for you to make the most informed decision for your products.

And that would be - you'd have to drill into the details about the information we had about the product, and that can probably be - I think to a high level be sought after via the pre-submission process. (Patrick), does that sound about right?

(Patrick): Yeah, it does. And, you know, and the pre-submission and the regulatory options table that is - you know, we basically would be sort of doing - you know, after you describe your thoughts and your plan to change the technology and maybe what you think would be a Denovo and what could fit under a 510K, you know we can sort of give you a regulatory options table that's basically an if/then statement, you know, saying if you take this approach, here's the type of claims that you would be able to make and here's the type of predicate that you would need and sort of be able to lay that out in a pretty granular and direct fashion.

So that's certainly something that we've seen in the past I can say. And we're happy to help you, you know, think about some of the nuances to that approach. I think that's it. (Unintelligible) to (Matt).

(Matt Trabella): Can I ask a follow-up question then? So with the Q submission process, we've gone through one round and submitted questions and had feedback from FDA. And we're at exactly this stage. How would we proceed with follow-on questions? Should we do a new Q submission or can we continue asking questions with the existing Q submission?

(Patrick): Yeah, (Matt). So what you would do - what you would generally do is submit a supplement to the previous Q submission and probably reference, you know directly reference some of the feedback that we provided and you know, say kind of what your - you know what you're planning to do based on the feedback.

Potentially just say, you know, it can be sort of a new thing, if you'd like it to be, but we're also - you know it can be a continuation of the feedback that you've previously given and sort of iterate on what's been done.

It's really up to you and what you're looking to get out of us. But (unintelligible), you submit a supplement to the Q submission and we receive it and go through the review process again. Was that helpful? Were there other questions, a question that I could help address?

(Matt Trabella): No, I think that's very good. Thank you.

(Patrick): Great.

Operator: Thank you. Our next question is from (Weaver Gang). Your line is open.

(Weaver Gang): So this question is if you started down the De Novo classification request pathway and then a PME is granted for a device that could serve as the predicate. Do you then get automatically transferred to 510(k)?

(Carlos): Yeah, that's a good question. I would - you know, if you have that scenario I would contact the lead reviewer that you've been assigned for that submission and see if you can have a quick update discussion on the review of your application. That would be one where we want you to contact the lead reviewer.

(Weaver Gang): Okay. Thank you.

Operator: Thank you. Our next question is from (Roger Faulkner). Your line is open.

(Roger Faulkner): The device that we've been working on is a negative pressure ventilator. It's got three major levels of risk application. Good news, asthmatic patients or people doing athletic training - to improve results it could be an ambulatory system for COPD where if it fails nobody dies. Or it could be for the case that I have. I have ALS and I need 24/7 ventilator support. It seems to me that one of those is class one, one is class two and one is class three.

Is there - I mean, I certainly could describe this in the review process, but my hope is to be able to start by addressing the (unintelligible) market and then move up towards doing, requiring absolutely reliable operation while in the suite, for example. Any comments helpful.

(Carlos): Yeah, so that's a great question because many times sponsors depending upon the - so (Patrick) and I will answer this in general, because this product is in another office but it's a great question. And I think you see parallels to products in the (unintelligible) space.

But many times sponsors, depending upon the datasets that they may have - they may have different data sets for their products based upon a different usage of their product. There may be different indications for use in different targeted patient populations.

There you would want to have a discussion with the agency about what the indication for use is most - you're most focused on and how to move ahead. And

it sounds like there may be three patients that you are targeting. Not sure about the data behind it. Not sure - we would need more information.

I certainly want you to speak to our colleagues in the general hospital office. But it sounds like, you know, there could be a discussion had about the indications that you're most interested first and foremost immediately, and what data sets would be also needed for that indication for use that you're pursuing.

But sounds like there could be three patient groups and we sort of encourage you to look at the regulatory options that you hear from our colleagues about that product. That's sort of a first impression. And second comment would be we definitely want to match you up with the staff here at the center. And so if you can reach out to (Patrick) or I - we certainly could also help you connect with the right folks to better explore that scenario. But (Patrick), anything additional on your side?

(Patrick): No, I think that's exactly - we might have the same product but based on the intended use or the risks of those uses to the patient population specific to that use, you know, it could be regulated differently and would have different associated data requirements. Nothing to add on top of that.

(Roger Faulkner): May I have a follow-up question with this? I've identified a prior device that's already been through the De Novo process. (Unintelligible) pretty close to my device, it's just it uses a rigid (unintelligible) instead of a vest that basically moves with you. I have been able to find any information other than the very fact that it exists. Whenever somebody files a De Novo is that public information, and if so how do I find it?

Carlo: Yeah, so (Patrick) you want to start us off, or you want me to take this one?

(Patrick): Yeah, I can get started. At least to your second question, all of our De Novos are - we provide public information about how they provided (unintelligible) summary that goes over at some level the type of information that we considered to come to our recommendation about granting the De Novo and

that includes, you know, information about the type of device, the clinical data, the bench testing, the benefits and risks, the special controls and all of that.

It's available somewhere on the website. If you were to follow up with our site that was linked on the previous e-mail or follow up with any the . . .

(Carlos): (Patrick), did we lose you? I think we might have lost (Patrick) but sir, I think if you send a note to Dice that they have their e-mail address, their e-mail address is on the slide here. And then I'd be happy to - you know if you send me an e-mail, (Carlos).Pena@fda.hhs.gov, I'd be happy to make sure you get the right (unintelligible) folks here at the center. (Unintelligible) the right office here.

(Roger Faulkner): Thank you, (Carlos).

(Carlos): Sure, no problem.

Woman: We'll go ahead and go to our next question. The operator is also checking. Okay, he's back.

Operator: Our next question is from (Henry Monca). Your line is open.

(Henry Monca): Hi, this is (Henry) again want to thank you all for taking the time out of your day to give this very helpful webinar and have this discussion today. I think my question got converted into a follow up so maybe it will be quick. I wanted to follow up on the notion of including human clinical data if it happens to be available in the (unintelligible). Again on the slides, hey you really didn't want it and I suppose I can understand why.

But then there was a follow-up question which I heard a bit of and I apologize, (unintelligible) in which you said hey maybe if there is some human data available at the time of the pre-sub, again we all understand the pre-sub is not intended to be the De Novo submission itself.

But if there is human clinical data at the time of the pre-sub, what are the

circumstances in which you want to see it and maybe what are the circumstances under which you'd rather not. Maybe that would help us make a helpful decision there. Thank you.

(Carlos): Yeah, so that's a great question. Maybe we don't typically evaluate data in a pre-submission because that would be sort of a - you know, it's really more appropriate for us assembling our limited resources to look at the actual marketing submission. But sometimes it's hard not to look at something. Kind of like, you know, when you - it's hard not to look at the data that's contained in a submission.

So I think if you're trying to give us a helpful hand in exploring your product in some of the data you have, I would go ahead and include as much information you think is going to be useful for us to have a productive discussion. And many times - you know sometimes we just - we take a little peek at the next couple of pages of data.

We try not to structure the discussion that way but I think if you think it would be helpful to do more regular regulatory questions that you have, and you think that background would also be useful, I would go ahead. I would encourage a little bit more information than that when you have that available and at hand.

(Henry Monca): Okay, thanks, that's very helpful.

(Carlos): Sure.

Operator: Thank you. Our next question is from (Jason McEwen). Your line is open.

(Jason McEwen): Hi there, (Jason McEwen) here from (unintelligible), and we make (unintelligible) medical devices. I just wanted to ask the question on kind of a scenario that we've seen potentially coming up in the future. And that is, if we were to do a De Novo on a - hypothetically let's say a device that treats anxiety, and there's a new product called - issued by the De Novo. Then we subsequently want to use that exact same piece of technology, the same

characteristics, effectively an identical device but for an entirely different indication.

Hypothetically let's say something like Parkinson's disease. So exactly the same technology but two very distinct indications. Given that we have done the first De Novo, is that still a second De Novo for that second indication, or is that actually 510(k) given that the technology is identical?

(Carlos): (Patrick), you're back online. You want to take that, you want me to start?

(Patrick): Yeah, I can start with that. Sorry, my call got dropped. But thanks (Jason) for your question. So after the initial experience for anxiety, if you're using the same exact technology for a different indication for use, we would then have to determine whether it falls within the same intended use to determine whether the subsequent submission would be a potential 510(k) or potentially a De Novo.

And you know there's a lot involved in the determination of intended uses, you know the benefits and risks in the patient population. Are they similar? Are they different? Are there new risks to using the same product in a different patient population?

It's possible that it could be a 510(k), it could possibly be a De Novo. This was be very good topic for a pre-submission discussion because we would probably be able to give you some pretty good feedback as to whether that type of approach might be viable to, you know, get one clearance or get one device in De Novo and then use the same exact technology for a different indication for use.

So I would very strongly recommend bringing that type of question to a pre-submission. Especially since you know that would - there be multiple associated clinical studies for - might be some other indications for use. So that would be a substantial time investment on your end.

(Jason McEwen): Okay, excellent. Thank you.

(Patrick): Likely speaking at least.

(Jason McEwen): Thank you.

Operator: Thank you. Our next question is from (Nashear Dorey), your line is open.

(Nashear Dorey): Thank you so much for the opportunity and a clear and thorough presentation. My question is regarding the risk/benefit assessment again. Are there risks that are considered to be a no-go, for example with a brain (unintelligible) cortical implants because of the obvious risks associated with it. Do you always automatically categorize it as a class three risk even if it has probable as you mentioned survival benefit. Thank you.

(Carlos): Yeah I guess this is - I could start this off (Patrick). And you know we'd need a little bit more information about the use and the benefits versus the risks. But it would be - one point of discussion would be the risk of the device and how there may be comparable products out there that have been regulated.

I would want to have a little bit more information about the technology or you know what, additional information about the technology when and how it would be used, the proposed benefits, the risks. I mean this would be all types of information that could - definitely pre-submission but focus our (unintelligible) I think you're looking for from a CA. I think this is one that would really be a nice pre-submission pathway type of discussion.

Keeping in mind that the De Novo program is for low to moderate risk. It seems like we'd need to have a more in-depth discussion about where the line is on a moderate to high risk for your product or its use than the patient population targeted. Does that make sense?

(Nashear Dorey): Just to make sure I understand, by just virtue of something being implantable in the brain, that doesn't automatically mean we have high risk if they're really

providing high benefits. Just hypothetical and high level, or usually . . .

(Carlos): I would say there are no absolutes and I think this discussion - it would probably be good to have a pre-submission counselor here. There is no absolute. You'd have to talk a little bit more about the implantation, a little bit more. But I think we just need some more information before we could give some advice there. (Unintelligible) go with the pre-submission pathway or maybe the determination pathway. (Patrick), any thoughts?

(Patrick): No. I agree that, you know, a lot of the specifics about the implants, you know the site, the material, what it's doing, you know all of that kind of (unintelligible) the risks. It's obviously you consider implants are usually on the higher end of the risk spectrum. But I don't know if we would absolutely be able to determine, you know, whether they would automatically be subject to a PMA just due to the fact that it is implanted.

(Nashear Dorey): Thank you very much.

Operator: Thank you. Our next question is from (Allison Comiama). Ma'am, your line is open now.

(Allison Comiama): Thanks. I made it back to the front of the line. I have one other question. This is actually for (Sergio). Is there a set timeline for posting the decision summary to the FDA De Novo database? I know for some companies that are interested in using a previously granted device as a predicate, understanding what's needed to submit a case is helpful information to have. I just don't know if there's - like who generates that decision summary and is there any timeline that we can expect that to be posted. And thank you.

(Carlos): That's a good question (Allison) and, you know I think this is your second question so - but I don't think we have a set timeline. I think what we try to do is we try to focus as quickly as possible. There may be some special circumstances where we post things sooner than later just because, you know, we want to get that posting up for the community.

But I don't think we have a set timeline, but I think it's more of a - we try to focus as soon as possible with the resources that we have. But we can double-check and send you something off-line if there's a timeline set.

(Allison Comiama): Thank you for taking my question. I did get back in line but I appreciate your answering my question.

(Carlos): No, no problem.

(Allison Comiama): Yeah. Thank you so much.

Operator: We'll take our last question and that will be from (Henry Monca). Thank you very much.

(Henry Monca): So again thank you for staying on a few more minutes for a second question. And there was a lot of commentary during the slide talk, very helpful slide talk about how big the pre-sub meetings - one of the main goals is to have FDA have an understanding of what the device is.

So for software-based medical devices, where it's possible to provide a demo on the web or for example through the app store to FDA. Is it helpful to provide a way to FDA staff to demo the software to help further their understanding beyond bare screenshots? Or is that just not something that FDA prefers to do prior to pre-sub? Thanks.

(Carlos): (Patrick)?

(Patrick): Yeah, I think that's an interesting question. I think you know it probably depends on the individual review team involved. I certainly could see utility in having, setting up like a sub-meeting or a phone call or something for the company to kind of walk their review team through the software if that would be a more productive way to describe the technology and what it's doing, the user experience and all that. But I think reviewers would probably encourage

that and work with you if possible.

Obviously we'd still be looking for some type of skeleton description of the product to get things started and help us out at least in the initial part of it. But I think that would be something we'd encourage if that works for the company.

(Carlos): Yeah, and just to double (Patrick)'s comments. You know any time - just a few additional comments. One is that if there is an opportunity such as an informational meeting for all of us to get together with you and see a demo of the product or see the product through a video, through its use on patients or just have a real-life visual experience, that would be a really great opportunity for us to make sure we're all aligned on what you're seeing. That you make sure that you have us to see what you see about your product.

And then the second thing is, you know, if people think it's too early to contact the FDA that's exactly the time to contact the FDA. You know all too often sponsors come in after the study's been done, the data is now complete, and you didn't have a chance to talk about, you know, what will be maybe even the least burdensome approach to taking the product to the marketplace. There could be money saved, there could be, there could be steps that maybe weren't needed.

And, you know, in closing, if you think it's too early to contact us, that's the best time to contact us. And I think you'll be surprised with the engagement because we're really trying to make sure you all understand our expectations. And we all understand the device that, you know, you're in love with that we want to make sure gets changed for patients and their families. So, you know, I think engagement is the message here and that's going to help the promote this program be a success. Irene, I'll turn it back to you.

Irene Aihie: Thank you Carlos. And again, this is Irene right here and we appreciate your participation and thoughtful questions. Today's presentation and transcripts will be made available on the CDRH Web Page at www.FDA.gov/training/CDRHlearn by Friday. September 4th.

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

Operator: Today's event here has concluded. Again thank you for your participation. Please go ahead and disconnect. Thank you very much.

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