FDA Webinar - Regulatory Overview for Developers and Sponsors of Neurological Devices: An Introduction to the De Novo Pathway
Moderator: Irene Aihie
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Coordinator: Welcome and thank you for standing by. At this time all parties are in a listen-only mode until the question and answer segment at the end of today's conference. At which time you may press star one on your touch tone phone to ask a question.

I would also like to inform all parties that this call is being recorded. If you do have any objections, please disconnect at this time. I would now like to go ahead and turn today's call over to Ms. Irene Aihie. Ma'am, you may begin.

Irene Aihie: 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 effort 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 devices information on the De Novo pathway, an alternate pathway to classify novel devices automatically placed in class three and (requesting) classification into class one or two.

Dr. Carlos Pena -- Director of the Division of Neurological and Physical Medicine Devices in the Office of Device Evaluation here in CDRH -- will

start today's presentation. He is joined by members of the division. Following the presentation, we will open the lines for your questions related to information provided during the presentation.

Additionally, other Center subject matter experts will join the team to assist with the Q and A portion of the webinar. Now, I give you Carlos.

Dr. Carlos Pena: Thank you Irene. Good afternoon to folks on the east coast as well as folks that are joining domestically and abroad. I am delighted to welcome everyone to our second public webinar for neurological and physical medicine devices.

Today's session is focused on the De Novo pathway and will highlight some of the factors to consider when submitting a neurological or physical medicine device submission under the De Novo pathway. And there's a couple topics that we're going to be talking about today, which will include an introduction to the pathway, some of the regulatory history of the De Novo pathway, benefit-risk analysis, case study, the (expedited) access pathway program, engaging with the FDA through the pre-submission process and a few closing remarks.

Thank you, apologies for the delay. Our Division of Neurological and Physical Medicine Devices within the Office of Device Evaluation is within the Center for Devices -- one of several product centers at the agency. And the staff presenting to you today are from our very own Division of Neurological and Physical Medicine Devices. It is one of the newest divisions in the office and speaks to the investment of the - that the agency's making in this area.

At CDRH our vision is that patients in the US have access to high-quality, safe, and effective medical devices of public health importance first in the

world. And the medical device is defined as an instrument intended for use in the diagnosis or cure, mitigation, treatment, or prevention of disease, or 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 one can classify a device as a medical device even in the absence of claims when a device impacts the structure or function of the human body. We have been engaged for -- in the technology sector -- for some time and this is a favorite slide of mine. Here I show you an array of products with neurological indications.

Beginning with neuro thrombectomy devices, to ablation therapies for movement disorders, neuro-diagnostics, prosthetics to therapeutic devices for migraines, and micro-catheters for the neuro-vasculature. Many of these products treated the needs or condition. And the majority of products were authorized just in the last three years alone -- some of which went through the De Novo pathway.

The goal is not to discuss individual data in support of each device, but share with you here that each device went through a regulatory pathway that was, in part, tailored to the individual risk and benefit profile of that device. There are a number of regulatory pathways to bring a device to market.

And from a recent paper this division published in December we show here several of those pathways. Such as the pre-market approval pathway or PMA pathway, the pre-market notification pathway -- otherwise known as the 510(k) pathway -- and the De Novo pathway, which Mr. Michael Hoffmann will be discussing shortly.

I would also like to note that medical devices can be classified into three types. Two of which are listed here -- class two and class three -- and these are the higher risk classifications which can be linked to regulatory submission pathways.

So for example we receive several dozen PMAs each year. These submissions are the highest risk and require clinical data -- these are class three. A second pathway is the 510(k) submission pathway. We receive several thousand each year and they typically do not contain clinical data, but are supported by non-clinical data in bench testing and review of prior submissions that may have contained clinical data. These are typically class two.

Finally, the third regulatory pathway -- of interest to the current webinar -- is the De Novo submission process pathway. Which includes devices that aren't comparable to anything on the market and present a lower risk than other types of devices. Typically, once we have granted a De Novo, that particular product becomes the predicate to subsequent products which then can move along the 510(k) pathway.

We receive a number of De Novos across the division. And here I last show you the new organization of our division and distribution of products across each of the branches. As we now drill deeper into the De Novo process and I turn to Mr. Hoffmann, our regulatory policy deputy director for the division.

Michael Hoffmann: Thank you Carlos. Again my name is Michael Hoffmann and I will be discussing the regulatory aspects of the De Novo program.

So what is a De Novo? It is a risk-based approach to allow new, novel, low and moderate-risk devices to market in cases where there is no predicate

device. Without this provision, such devices would automatically be classified as class three. The De Novo process allows such devices to be classified into class one or class two.

The De Novo process is a classification process. A De Novo application is sent to FDA by a medical device sponsor or manufacturer. If the De Novo is granted, a new regulation for the device is created as well as a product code. It is given a classification -- one or two -- and necessary controls are identified. And this device is the first in that new regulation and device type, and becomes a potential predicate device for subsequent sponsors to compare their devices in future 510(k)s.

The Food, Drug, and Cosmetic Act was revised in 1997 to create the De Novo process. Section 513(f)(2) establishes the De Novo classification process and allows FDA to classify devices into class one or class two that were automatically classified into class three. They are classified into class one or two using criteria set forth in 513(A)(1) -- and please note that this excludes devices already classified into an existing regulation.

The De Novo process as laid out in 1997 necessitated that a device go through the 510(k) process first. A sponsor would submit a 510(k), and FDA in those cases would find the device NSE due to lack of a viable predicate. Meaning that the device presented either a new intended use and/or different typological questions when compared to the predicate device.

The sponsor would then - could then submit a De Novo request but had to do so within 30 days of receiving the NSE letter. FDA would then evaluate the information to determine if there was sufficient information to classify the device into class one or class two. The De Novo position was changed in

2012 with FDASIA. One of the key provisions is that a sponsor no longer had to submit a 510(k) and receive an NSE letter first.

A De Novo submission could be submitted directly. Additionally, the time frame for review was set to 120 days with the goal to streamline the process and increase efficiency. This allowed two methods for the De Novo pathway. The previous pathway -- which was the post-NSE through submitting a 510(k) first -- which is still a viable path. Or a direct submission of a De Novo submission.

However, all review standards and decision-making considerations are unchanged. When putting together your De Novo submission we strongly suggest that you include the following information. The first would be the regulatory history of your product, of your device. Have you had any prior submission of the device to FDA? Was there a prior 510(k) or a related NSE decision? Was there an IDE? Was there a pre-submission? Were there any previous De Novos for the device that were withdrawn or declined?

All this information facilitates review by allowing the review team to catch up with any applicable regulatory history and any previous information that may have been discussed with the agency. You should include the device name and device description, the intended use and indications for use, and the technological characteristics. These are very critical elements since they help us determine the risks of the device and define the patient population.

Similarly labeling needs to be included to instruct users how to use the device safely and effectively. If there are different sets of labeling for patients and professionals, please include both in your submission. You should also provide a classification summary. A review of similar classifications, regulations, product codes should be provided to demonstrate that this device

is eligible for a De Novo rather than a 510(k) or a PMA. This would normally be done in the 510(k) if one is submitted before the De Novo.

You should provide a proposed classification -- class one or class two -- and a justification. FDA will evaluate and make their conclusion on the class of the device based on the information provided. Similarly, you should propose special controls to mitigate the risks of your device. Note that this is applicable to class two devices only.

Special controls include items such as biocompatibility testing, electrical testing, (EMC) testing, as well as labeling. Class one devices do not need special controls because they are devices for which only general controls are sufficient to provide reasonable assurance of safety and effectiveness. General controls include labeling, good manufacturing practices, device reporting, and they are applicable to all devices.

You should also provide supporting evidence to demonstrate how your device -- with the special controls -- can provide a reasonable assurance of safety and effectiveness. You should provide the test methods as well as the results. The testing can include pre-clinical testing, animal testing, and clinical testing, where appropriate -- as well as the discussion of how those data correlate to the evidence and the proposed classification.

Our final decision is also based on the benefits of the device and the risks when used as labeled for the indicated population. Therefore, you should provide a discussion of both the probable benefits to health as well as the known and probable risks to health.

You should discuss what mitigations are in place to address the various risks of the device. You should also discuss how the benefits -- with the

mitigations and special controls -- outweigh the risks for the proposed patient population.

There are several different types and ways of thinking about benefits as well as risks. For that discussion I will hand the presentation over to Leigh.

Leigh Anderson: Thank you. Hello, my name is Leigh Anderson and I will be presenting a brief summary about benefit-risk determinations.

As part of the De Novo review process, FDA evaluates both the benefits and the risks of the device as part of a benefit-risk determination. You can access FDA's guidance document entitled "Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications" using the link at the bottom of this slide.

This guidance document is a helpful resource that explains the principal factors the FDA considers when making benefit-risk determinations during the pre-market review of PMA or De Novo submissions, with De Novo submissions the focus of today's presentation.

As part of the benefit-risk determination for a particular device, FDA must balance the probable benefits and probable risks when determining a reasonable assurance of safety and effectiveness of the device for its intended use. As we are focusing on the De Novo review process today, please note that since devices classified under the De Novo review pathway are considered low to moderate risk devices, they may not need to confer as substantial a benefit to patients in order to have a favorable benefit-risk profile.

Both clinical and non-clinical data can play a role in the benefit-risk determination for a device. Non-clinical testing could include a variety of methods -- such as animal studies, mechanical testing, electrical safety testing, sterility, and shelf-life testing -- which can also provide important information to consider in the pre-market review and benefit-risk determination for a device.

For De Novo requests, FDA relies on valid scientific evidence to ensure we sufficiently understand all the risks and benefits of the device to confirm all risk can be appropriately mitigated with general and/or special controls, to provide a reasonable assurance of safety and effectiveness.

We've noted that FDA must determine that there's a reasonable assurance of safety and effectiveness. Specifically, a reasonable assurance of safety occurs when it can be determined, based on valid scientific evidence, that the probable benefits outweigh any probable risk, and we can establish the absence of unreasonable risk of illness or injury with the use of the device for its intended use and conditions. In addition, a reasonable assurance of effectiveness occurs when it can be determined -- based upon valid scientific evidence -- that the use of the device for its intended use will provide clinically significant results.

We've noted that FDA relies on valid scientific evidence when making benefit-risk determinations. This can include information from a variety of sources, including evidence from well-controlled investigations; partially controlled studies; studies and objective trials without match controls; well-documented case histories conducted by qualified experts; and reports of significant human experience with the marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is a

reasonable assurance of the safety and effectiveness of the device under its conditions of use.

–Please note that in general, isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence for supporting safety or effectiveness. However, this type of information may be considered in identifying a device with questionable safety and effectiveness.

As we noted earlier, FDA must balance considerations of both probable benefits and probable risks to determine that the probable benefits outweigh the probable risks and to ensure that all risks are appropriately mitigated with general and/or special controls for De Novo classifications.

A variety of factors are considered for evaluating the extent of the benefit and risk of the device, and FDA considers each of these factors individually and in aggregate, to reach a benefit-risk determination for the device under review.

Factors that FDA considers when evaluating benefits include the type of benefit, the magnitude of the benefit, the probability of the patient experiencing a benefit, and the duration of the treatment effect.

For each of these factors, FDA considers a variety of questions when evaluating the benefits of the device. For instance, FDA considers the primary, secondary, or surrogate endpoints evaluated in the clinical study, and the type of value that patients place on the benefit, as well as the magnitude of the treatment effect and how the benefit ranks on the scale used to measure the benefits.

FDA also considers the probability that the patient will experience a benefit with use of the device, which may include considering how the benefits vary across sub-populations, or if the study could predict which patients would experience a benefit. Finally, FDA considers the duration of the treatment effect and the value to patients associated with the duration of this benefit.

Similarly, FDA also considers a variety of questions when evaluating each factor related to the probable risks or harms with use of the device. For instance, FDA considers the device-related serious and non-serious adverse events, as well as procedure-related complications, when evaluating the severity, type, number, and rates of harmful events.

FDA evaluates the probability of a harmful event, considering the incidence of each harmful event in the population, as well as the uncertainty in that estimate. and, if applicable, whether the incidence of harmful events varies by sub-population. FDA also considers whether patients would be willing to accept the probable risk of the harmful event given the probable benefit of the device.

When evaluating the duration of the harmful event, FDA considers how long the event lasts, whether or not it is reversible, and the types of intervention needed to address the harmful event. For diagnostic devices, FDA also considers the risk from a false-positive or a false-negative result with use of the device, and whether or not the device is the only means of diagnosing the problem, or if it is part of an overall diagnostic plan.

In addition to the benefit-risk factors noted earlier, FDA also considers a variety of additional factors when evaluating the overall probable benefits and risks of the device. For example, FDA considers the degree of certainty of the benefits and risks of the device, which includes considering the quality of the

study design, study conduct, robustness of analysis, and the generalizability of the results.

FDA also considers the characterization of the disease and the availability of alternative treatments or diagnostics, including considerations of the effectiveness and risks of alternative treatments, and how well currently available therapies already meet the medical need the device addresses.

FDA may also consider additional ways to mitigate risk, such as limiting the indication to a subset of the population in which the benefits outweigh the risks, or using product labeling to further mitigate risks. Furthermore, FDA also considers patient perspectives, which may include any patient-centric assessments, patient reported outcomes, or patient preference information available for the device submission.

For more details of the specific types of questions that FDA considers when evaluating each of these additional factors, I suggest you refer to the benefit-risk guidance document cited earlier in this presentation for further reference. Now I will turn the presentation to Kristen Bowsher who will provide an overview of a hypothetical De Novo case study.

Kristen Bowsher: Hi, I'm Kristen Bowsher. I'm going to walk you through some of the key aspects of a hypothetical case study that describes the steps in determining whether a device qualifies for a De Novo submission. You can find this case study on the FDA web page provided on this slide, and you can also find it through a link on the webinar webpage.

We recommend that you read through the case study,including its appendices, which include references and links to other FDA documents,such as guidance documents, that will also be very useful to you. At this point you may want to

access the case study from the webinar website. In particular, later in my talk I will be referring to table one on page five.

The first step in the process of determining whether a device qualifies for a De Novo submission is to define the technology and the intended use. These are the key criteria that determine whether your product is a medical device. And if so whether it is eligible to be clear for marketing through a 510(k) or must be evaluated in a De Novo or PMA submission.

The hypothetical device we are going to discuss today is called the DailyStim. Technologically, the DailyStim is a portable AC powered trans-cranial magnetic stimulator -- or TMS device -- that externally delivers directed, brief-duration pulse magnetic fields to induce electric currents in specific regions of the brain.

The intended use of the DailyStim is as an adjunctive therapy to aid in reducing the symptoms of advanced levodopa-responsive Parkinson's disease that are not adequately controlled with medication. Note that the term "intended use" refers to the general purpose of the device or its function.

The term "indications for use" is encompassed by the intended use. And describes the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient population for which the device is intended. The indications for use for the DailyStim is as an adjunctive therapy to reduce the severity and frequency of tremors in adult patients with advanced Parkinson's.

Step two is to determine whether the device is regulated as a medical device. Dr. Pena discussed the criteria in this slide in his presentation. Based on both the technology and intended use, I think it is pretty apparent that the

DailyStim is a medical device as it is intended for use in the treatment of a disease or condition -- that is Parkinson's disease. And it is also intended to affect the function of the body through electrical stimulation of the brain. Note that either one of these make it a medical device and both are not required.

Step three in determining whether the De Novo is the appropriate pathway for the DailyStim is to find out if there are any similar products currently cleared for marketing under a 510(k) or De Novo that would serve as a predicate device. Or if there is a similar device already being legally marketed under a PMA.

In step one I defined the technology and intended use of the DailyStim. And as a next step, I am looking for legally marketed devices in which both the technology and the intended use are similar to the DailyStim. This is done because if there is a legally marketed predicate device that is similar, then the 510(k) substantial equivalence pathway -- not the De Novo -- is the appropriate pathway.

Likewise, if there is a similar PMA approved device then an appropriate class three regulation exists,nd either a PMA submission or a reclassification petition -- not a De Novo -- is appropriate. So how do you go about determining whether there is a legally marketed predicate device or PMA-approved device that is similar?

FDA provides several public databases to help in your search. These databases can be found by going to the Classify Your Medical Device webpage, which discusses various search methods you can use and provides links to several databases to use in your search. I will note at this point that if you ultimately determine that your device does qualify as a De Novo, your

searches of the FDA public databases and other resources -- including search terms used to establish that no legally marketed device of the same type exists -- will need to be provided in your De Novo submission.

The databases that can be linked to from the Classify Your Medical Device webpage include the product classification database shown in this slide. Additional useful databases for classifying your medical device can be linked to from this database -- as shown circled in green on the right side of this slide -- and they include the 510(k), the De Novo, and the PMA database.

In the product classification database one can search on a variety of parameters such as device, product code, review panel, regulation number, and submission type. To obtain the most thorough search results I suggest searching under device and using broad search terms, searching on only one search term at a time.

For example, for the DailyStim I might search on the device term "trans-cranial," circled in red on this slide. And then do a separate search on the term "Parkinson's." Search results bring up device types including the search - that include the search term in their name and their associated product code, regulation number, and device class.

Once I have the product code I can find whether a device is cleared or approved under that product code by performing searches under the 510(k), De Novo, or PMA database. Let's first examine the results using the search term "trans-cranial" in the product classification database for the DailyStim example. The top portion of the slide depicts the results.

One of the product codes that results from this search is the OKT product code -- which is a class two device -- which is a trans-cranial magnetic stimulator

for the treatment of migraine headaches. This result links to a page that describes the regulation definition that includes the intended use and technology in more detail. Note that one would follow the same steps I will discuss now for the OBP product code as well.

If we take the OKT product code and enter it into the De Novo database, we can find a specific De Novo submission number associated with this product code. In this case -- as depicted in the bottom section of this slide -- we find the Neuralieve Cerena device had a De Novo granted under submission number DEN130022.

A link from this page is provided to the decision summary which includes the indications for use and the technological description of the device. It also includes the data which FDA used to grant the De Novo.

A summary of the data.

Referring to the decision summary in Table One from the FDA case study for the hypothetical DailyStim we see that the intended use for the Cerena is for the acute treatment of pain associated with migraine headache with aura. And that the technology is an AC-powered device that delivers a brief pulse of magnetic energy to the back of the head to induce electrical currents in the brain.

So, how similar does the DailyStim need to be to the predicate device -- in this case the Cerena -- to be determined substantially equivalent? This slide shows the key decision points in the 510(k) decision-making flowchart which depicts the logic used by FDA for determining substantial equivalence. It is depicted in Figure One in the FDA case study. And also can be found in FDA's 510(k) guidance document entitled The 510(k) Program: Evaluating Substantial

Equivalence in Pre-Market Notification, which I refer you to for more in-depth discussions and for several examples using the decision flowchart.

The intended use and the technology characteristics are the two major attributes FDA uses to determine whether a predicate exists. Let's now step through the decision points to compare the DailyStim to the Cerena. Decision one asks whether the predicate device -- in this case the Cerena -- is legally marketed. We've already done our database search and determined that a De Novo was granted for marketing for this device. So the answer here is yes.

Decision two asks whether the DailyStim has the same intended use as the Cerena. We can refer back to table one in the FDA case study and see that the (DailyStim) is intended to treat tremor in patients with Parkinson's disease while our database search found that the Cerena is used to treat pain in patients having migraines. It was pretty clear that these intended uses are not the same. And according to the flowchart an NSE -- or not substantially equivalent -- decision would be made.

Therefore, the Cerena is not an appropriate predicate device. And at this point you do not need to go further down the flowchart to compare their technologies. So in this slide we have determined the Cerena is not an appropriate predicate device. Now let's examine the results from using the search term "Parkinson" in the product classification database.

The results from using the search term "Parkinson" in the database showed two product codes, both for class three devices. There's MHY - product code MHY for an implanted electrical stimulator for Parkinsonian tremor. And NHL for bi-lateral stimulation of the internal globus pallidus or subthalamic nucleus for adjunctive therapy in reducing some of the symptoms of Parkinson's disease.

Note that Table one in the FDA case study lists the MHY product codes but includes the NHL description. In this case however it is the same device technology. We can then enter the product code NHL into the PMA database and the search produces the Medtronic Activa Parkinson's control system -- approved under PMA number PN60009, supplement seven.

The result also links to a page that allows you to access the summary of safety and effectiveness data on which the device was approved. This summary includes the intended use and a description of the technology, which we can then use to compare to the DailyStim. This comparison is depicted in Table one of the FDA case study.

You see that the Medtronic Activa Parkinson's control system is a class three implanted neuro-stimulator for the bi-lateral stimulation of the internal globus pallidus or the subthalamic nucleus for the adjunctive therapy in treating some of the symptoms of Parkinson's disease. Now we need to determine whether the DailyStim is similar to this invasive device. In this case the intended use of the DailyStim is very similar to the Medtronic Activa device in that both are adjunctive therapies for reducing symptoms of Parkinson's disease.

However, the Medtronic Activa is a device that is a high risk device that is implanted into the brain while the DailyStim is an external stimulating device. It appears that the DailyStim presents a lower risk in which a combination of general and special controls should be sufficient to provide a reasonable assurance of DailyStim's safety and effectiveness.

In the next slide I'll discuss how to assess the risk of the DailyStim. The question to ask when determining whether the DailyStim is a high risk or moderate to low risk device that would qualify for a De Novo is, can general

controls or a combination of general and special controls ensure reasonable assurance of safety and effectiveness?

In order for the FDA to evaluate whether the DailyStim is a low to moderate risk device you should sufficiently understand and be able to explain all of the known risks and benefits of the device. As well as how all the known risks can be effectively mitigated, and device effectiveness can be assured through the application of general controls, or general and special controls.

Depending on how similar the devices are, the special controls used for the Cerena device could provide a useful guide to many of the special controls for our hypothetical DailyStim device. However, special controls cannot be fully defined until all valid scientific evidence -- including any necessary clinical data -- is collected.

Examples of special controls might include clinical and/or bench testing, labelling to mitigate risks of ineffective treatments, labelling to mitigate risks of ineffective treatment, seizures, adverse tissue reactions, or electrical shock. One of the first things you should do in making this assessment is to create a risk assessment of your device and create a risk management plan to address all the risks associated with your device.

We recommend you do the best you can with the device search for similar devices. But in order to get FDA's preliminary assessment of whether the FDA considers the De Novo pathway as an appropriate pathway you can also submit a request for a formal determination regarding whether the De Novo process is appropriate. You do this through a 513(g) request.

This provision states that FDA has a 60-day window to provide a determination regarding the classification and regulatory requirements

applicable to a given device. I refer you to appendix A of the FDA case study for more information. The FDA has a guidance document on the procedures you should follow for 513(g) requests and I recommend that you use this to prepare any such requests.

Besides -- or in addition to -- the 513(g) request you can also request informal feedback from the FDA on specific questions through a type of Q-submission. More information on this process will be discussed later in this webinar. I would note that neither of these submissions represent a final FDA decision, but rather represent FDA's current thinking based on the information provided in the submission at that time.

The fictional characters associated with the hypothetical DailyStim device submitted a 513(g) request. And based on that information they provided in a submission to the FDA, the FDA determined a De Novo pathway may be appropriate for that DailyStim device. After the De Novo is submitted to the FDA, the FDA will also perform its own classification review to confirm that the De Novo is the appropriate route to market.

After that, the FDA begins our substantive review. This includes making sure all the appropriate sections are provided, and performing a benefit-risk determination as discussed previously in this webinar. What happens after the FDA grants a De Novo? The new device is now legally marketed. It also is subject to any post-market requirements applicable to that device and class, including general controls, special controls as applicable.

The new device establishes a new classification regulation, and FDA publishes an order in the federal register which results in codification as the device's identification, classification, and applicable requirements including

general and special controls. The new device is now eligible to serve as a predicate device.

Of note, FDA also generates a decision summary that is publicly available on the CDRH website. This summary includes a summary of the information used to grant the De Novo. Again I would recommend that you look at the FDA case study on the FDA web page as it contains a lot of very useful information, including the case study itself, recommended information for De Novo and 513(g) submissions and links to relevant FDA guidance documents that should help you in developing a submission.

I now turn the presentation over to Lieutenant Commander Avena Russell.

Avena Russell: Good afternoon. My name is Lieutenant Commander Avena Russell and I will be discussing the expedited access pathway program. Also known as EAP program.

Recently there have been some changes made to the EAP program due to the 21st Century Cures Act. My presentation today will cover the new program structure as it relates to those changes.

What is the expedited access pathway program? The EAP program is a relatively new program that was implemented by the agency in 2015 as an effort to help expedite and bring novel technologies to market.

This program is strictly voluntary) and program participation must be requested by the sponsor via the pre-submission process in order to be considered for an EAP designation. Program eligibility is not for all medical devices. There is a defined program criteria that must be met for the pre-

submission to receive an EAP designation. This criteria will be discussed further in the next few slides.

If an EAP designation is granted during the pre-submission process, please be aware that this designation will follow an application submission throughout the review process. Applications eligible to qualify for the EAP program are pre-market applications - pre-market approval applications -- also known as PMAs -- De Novo requests, and 510(k) submissions.

The program eligibility criteria. To be eligible for an EAP designation your device must provide for a more effective treatment or diagnosis of a life-threatening or irreversible debilitating human disease or condition. When considering whether to submit a pre-submission request for an EAP designation you should first assess if your device provides for a more effective diagnosis - treatment, or diagnosis of a life-threatening or irreversible debilitating human disease or condition.

If your answer to this question is no, then it will not be eligible for an EAP designation. But will be eligible for another FDA regulatory pathway. However, if your answer is yes to this question when completing your pre-submission request please specify why, in detail, how your device adequately meets this criteria.

Eligibility criteria two. Once your device has been found to successfully meet criteria one, your device must then be assessed to meet one of the following criteria in order to receive an - in criteria two in order to receive an EAP designation. Criteria two. The device must meet at least one of the following criteria in order to be considered.

One, the device represents a breakthrough technology. And/or two, no approved or clear alternative devices exist. And/or three, the device offers clinically meaningful advantages over existing approved or cleared alternatives. Including the potential when compared to existing approved alternatives to reduce or eliminate the need for hospitalization, improved patient quality of life, facilitate patients' ability to manage their own care -- such as through direct - such as through self-directed personal assistance -- or establish long-term clinical effectiveness.

And/or four, the availability of the device is in the best interest of the patient. It is important to note that your device may meet one or more of the criteria specified above. However, it only needs to meet one in order to be eligible for an EAP designation.

It is also important to note that if you believe that your device meets this criteria, your pre-submission application should fully discuss the criteria and support how and why for each of the criteria. Again, in order to be eligible only one criteria needs to be met from those specified above.

EAP program eligibility criteria continued. For some of you, you may have previously submitted an EAP designation request prior to the new program changes. A draft data development plan was required during that time. However, under the new program changes submissions of a draft DDP is no longer required for an EAP designation.

A DDP is optional for sponsors to submit for those who request to receive a designation. For those who choose to include a DDP in their pre-submission request for designation, your DDP should outline the following: The clinical and non-clinical data that would be collected pre-market - during pre-market

and post-market, the analysis plan for each, and if applicable the analytical method for combining the two.

It also should include a timeline for the development and marketing of the device as well as for the post-market data collection. So please keep in mind again this information's optional and is not required in your pre-submission in order to request an EAP designation.

There are some features of the EAP program. Once an EAP request is submitted the sponsor will receive a grant denied or additional information requested - request letter. This letter will be received within 30 days once CDRH has received the designation. And a final decision to grant or deny will be made within 60 days.

If you've received an EAP designation, the designation will offer the following: Increased interactive review with the review team, increased senior management involvement, a designated case manager to help navigate the FDA, and a priority review. Additional information regarding the pre-submission process will be discussed by my colleague Patrick Antkowiak.

Patrick Antkowiak: Thanks Avena. Hi, I'm Patrick Antkowiak and I'll discuss some best practices for preparing a pre-submission for your De Novo device.

Much of the information I'll be discussing is described in the pre-submission program guidance document which is accessible at the link on this slide. And while that guidance document covers multiple types of interactions, today I'll focus on the pre-submissions. Now pre-submissions represent an opportunity to interact with FDA and obtain feedback on many aspects of your device, and will likely be the most relevant for you prior to your De Novo marketing application. Since pre-submissions have submissions numbers that always

begin with the letter Q you may have also heard these described in the webinar today as Q-subs.

The pre-submission guidance outlines the time frames for pre-submission review. If you request to hold a meeting with us, we'll strive to have that meeting within 75 to 90 days of the acknowledged receipt of your pre-submission. We'll aim to provide you with written feedback around three days in advance of your scheduled meeting date.

After you receive this written feedback, if you have no further questions you are certainly welcome to cancel the meeting. I'll note that typically we won't be able to have a meeting earlier than that 75-day time frame due to the workload considerations for our review staff. We urge you to budget your meeting time accordingly for one-hour meetings as we're generally unable to hold meetings longer than an hour.

And I'd like to point out that you can engage with us in a pre-submission while your device is still in early phases of development. We believe that early FDA engagement with a pre-submission represents a chance to identify potential issues and address them appropriately. This can be particularly helpful if you have very novel device technology, or if you'll need substantial testing or clinical data to support your device’s performance claims.

After an initial pre-submission, you're always welcome to submit a supplement at a later stage in your device's development if you'd like feedback then.

The one common issue that sponsors may have with pre-submissions is having them in a correct e-copy format. In order for your pre-submission to

be logged in and reviewed, your submission will have to comply with the e-copy guidance linked here.

If you don't comply with this e-copy guidance your submission will not be logged in and will not be reviewed until we receive a valid e-copy. For any questions about the e-copy format I'll refer you to the email address listed at the bottom of this slide.

So what should your pre-submission contain? At a minimum, you'll need a cover letter, background information on your device -- that could include device description, intended use, sanctioned animal testing protocols or clinical protocols. And you'll also need specific questions for FDA to address. More on those in a little while.

Please note that you should not include data such as data from a clinical study that you may have conducted. It is our policy not to review data in a pre-submission. For a De Novo pre-submission we additionally recommend submitting some of the information that Mike, Leigh, and Kristen described in this webinar including a proposed device class, a discussion of the relevant existing device regulations (and why you believe your device wouldn't fall into those), a risk analysis, and proposed special controls that mitigate those risks.

Another common issue that we've seen is the submission not including enough information up front. While we do recommend that you engage us early in your device development process we believe that at a minimum you should have identified your device's intended use and key design aspects before sending us a pre-submission. Please be mindful that a lack of upfront device description information -- especially for devices with novel technologies or

that we don't have a history with -- may hinder the chance to have a meaningful discussion.

So if your device - if your submission doesn't provide enough information up front about your device to understand how it works and how you intend it to be used, we'll end up asking you a lot of questions, which will take time for you to provide complete answers to. This ends up extending the overall length of the pre-submission review.

So remember that you're the expert on your device and you know the most about its technology. The more you can explain your device technology and your rationale for how you've developed -- or plan to develop it -- the better. Then we will be able to focus on giving you better feedback.

We also urge you to understand the existing landscape by searching for and reviewing applicable FDA guidance documents and consensus standards. Many of these are cross-cutting such as biocompatibility and software. So while your technology may be novel as a De Novo device, it helps us understand it better if you can explain what you're proposing in the context of standard guidance documents or similar device types that we have a history with.

So when it comes to providing background information our general rule of thumb is that more is better as long as it's organized. In our experience it's better to err on the side providing more information than you think we would need. If you're citing literature articles to support your device parameters or clinical study design, please include copies of those in your submissions.

Now with this being said, there certainly is such a thing as providing us with too much information. If you send us detailed circuit diagrams or thousands

of lines of software code or a copy of the entire grant that you used to support your device, that's more information than we would need to understand your device to answer your pre-submission questions.

We also recommend that you avoid making assumptions when providing us your background information. Unless there's an applicable guidance, standard, or other regulatory precedent, we recommend that you identify the most appropriate approach for your needs and provide some justification for it.

As an example, let's say that you plan to support your device's safety with an animal study. Well, not every animal study needs to use a non-human primate model. Another model or approach may be more acceptable provided that you can supply information that justifies that model and the protocol for your particular situation.

Now in your submission you should include - you should ask us specific questions to which we'll provide feedback. The most common issue 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 the answer to "What animal model should we use?" or "What should our clinical control group be?" We believe that those are your responsibility to determine and provide a justification to.

And as we noted earlier we also won't be able to answer questions about data review such as "Does FDA have any comments on the non-clinical test results?" In general, we believe that the best specific questions build on the background information you provided and include a proposal for us to review.

For example, say you provide an animal model with a rationale in your submissions. A good specific question for that could be "What concerns does FDA have with our proposed animal model?" We are happy to give you feedback on that. And similarly, if you describe your clinical control group the question that we'd be able to provide feedback on is "Is the selected control group in our proposed clinical trial appropriate?"

And finally here are a few appropriate specific questions for a De Novo device that are broadly applicable to a variety of device types. You could ask, "Based on the information provided does FDA agree that my device is eligible for a De Novo submission?" Or you could ask "Does FDA believe that there are risks other than the ones we've identified that must be mitigated?" Or "Are there any other special controls that should be considered to provide a reasonable assurance of safety and effectiveness?"

So in summary I'd like to again recommend that you engage with us in a pre-submission as early as is practical for you. I'll now turn it back over to Dr. Pena for some closing remarks.

Dr. Carlos Pena: Great, thank you. So a few closing remarks for this webinar. As we just discussed, pre-submissions are one of the best way to engage FDA. Not only do they allow for an opportunity to engage our staff about your device, but sponsors, developers, and innovators not only send more about the pathway for their product but can help exact investments, help make business decisions, and have realistic expectations about next steps in moving their products to the market place.

We spent a lot of time on sharing with you a variety of ways to learn about FDA. From recent articles to links to publications to websites online to our webinars -- there are a number of sources that we can also provide attendees

of this webinar today to learn more about how to best engage the FDA and the Center for Devices, our division specifically.

And one last comment about navigating the regulatory landscape for neurological devices. And first I would urge folks to find out more about us and about how to engage with us about your products. There are numerous pathways available. Two, if you think it's too early to contact us, that is exactly the right time to contact us.

Whether it's about non-clinical work needed to move to clinical studies, the right clinical study to gather data about your device, or the requirements to move your product to marketplace, this is the ideal time before that work has been started -- to engage with the FDA.

And three, call us. The more communication we have the better off you are in moving your products to patients and caregivers. And I think you'll be pleasantly surprised about your engagement with the FDA. So with that I'd like to close the prepared presentation that we have for the webinar and open it to questions from the attendees that are part of this session.

And I could even lead off with one question. One question could be from folks, what if my device is not a significant risk device, does it necessary - it doesn't necessarily require oversight of the FDA perhaps. Should I still come and talk to the FDA about how to collect the data for that product to support a marketing submission? And I will turn to Patrick to help us answer that question.

Patrick Antkowiak: Yes, thanks Dr. Pena. So the answer to that question is 100% absolutely yes. Even if you have a non-significant risk device please come in, send us a pre-submission that asks specific questions about your device. We'll be able to

give you feedback on things like your clinical trial design, clinical end-points, the patient population.

And these are all things that if they aren't done appropriately could potentially result in us asking for you to perform a new clinical trial. We can also give feedback on the bench testing and any kind of standards conformance that you'll need to support your device.

So yes, we wholeheartedly recommend coming in even if you have a non-significant risk device.

Dr. Carlos Pena: Thank you.

Coordinator: And if you would like to ask a question from the phone line it is star one and record your name when prompted. Again, that's star one and record your name when prompted if you would like to ask a question from the phone line. It'll be just a few moments for those to come through.

We do have a question standing by from Mark McCarty. Sir, your line is open.

Mark McCarty: Hi, thank you very much for taking my question. Patrick you said something about pre-submission filing including key design aspect. And I was wondering if you all have had enough experience with previous neurological device filings, you know, of a moderate risk nature I guess maybe try to (lift) PMAs? Because -- it might become a somewhat different discussion -- but maybe you can and answer in that context. About filings that you've had where the design elements were maybe sort of right on the edge of being sufficiently fleshed out for your - to a degree which you think is appropriate

and other instances where it was close but maybe not quite sufficiently fleshed out. Can you talk a little bit about that?

Patrick Antkowiak: Yes. So thanks for the question. Even if you're not entirely sure about your device's design and where it may end up we can still give you feedback - the best feedback that we can based on information that you have and how you plan to develop your device in the future.

And we might be able to give you tips on things that we would want to see from the design standpoint. So, you know, again this, the kind of the refrain is like Dr. Pena said, if you think it's too early to send us the pre-submission that's the right time to send us the pre-submission.

Mark McCarty: Okay. So it's not as though something's likely to have to back to an early feasibility study. If it's a De Novo type filing. Is that a reasonable assumption?

Dr. Carlos Pena: You know, I think the question probably would involve a little bit more information from you about you know, the device specifically, the technology, the indication.

That could be - that with additional information about your product, we can best navigate you to what stage you might need to engage FDA. There may be devices that you have that may not require as much investment depending upon a lot of different factors. But then there are other products that would.

And so it really depends upon more of the specifics but even, you know, even if you are considering whether to engage us -- even sending us a phone or an email -- in the pre - you know, before getting to a pre-submission would I think be very valuable to you and would help us help you.

Mark McCarty: Okay. Thank you very much. I appreciate it.

Irene Aihie: We'll take our next question.

Coordinator: Our next question comes from Shrie Couscyk. Your line is open.

Shrie Couscyk: Hi. Thank you for taking my call. I have a question to Lieutenant Commander Avena. You mentioned on Slide 47 that EAP process will be - will -- you can also do a 510(k) under an EAP process. But then again in 49 it clearly says no approved or cleared alternatives exist. Can you tell us where you might actually use a 510(k) for EAP designated device? Where would you issue a 510(k)?

Avena Russell: So currently the - it would depend on your device. And so you would have to submit a pre-submission in order to obtain a designation. But currently the program is steadily evolving and these are the new changes that just recently were implemented.

So in order to – so we couldn't really fully answer that question right now. You would really have to submit a pre-submission requesting EAP designation in order for us to fully be able to answer that question.

Shrie Couscyk: And what does that entail? Because I know this for a fact that we have a - we have devices that have been granted the EAP prior to 21st Century's Act being signed. And essentially that has taken us for the continuous interactive review pre-IDE and everything.

How does - and so you don't think you may be able to answer how this is going to help a 510(k) process in any shape or form? Because that's the

change that came out of the 21st Century's Act. And I was looking for some clarifications on that.

Avena Russell: So that was just only one of the changes that came out of 21st Century Act. So there were several changes that was implemented within the EAP program. That also included our program criteria, that was changed in addition to adding the 510(k) submissions, as well as the removal of the draft data development plan.

So again that's why we would encourage you to submit a pre-submission and as we are continuing to implement those changes we can better assess your question and your device technology.

Shrie Couscyk: Thank you.

Coordinator: Thank you. Our next question comes from Isabelle Common-Poulard. Your line is open.

Isabelle Common-Poulard: Yes, thank you very much for taking the question. My question is for Avena Russell. I would like to know if the EAP program is also open for companion diagnostics.

Avena Russell: Again you would need to submit your application because it would depend on the whole technology as a whole as well as what your device intended to treat. So you would have to submit a pre-submission in order for us to fully be able to answer that question.

Isabelle Common-Poulard: Thank you.

Coordinator: Thank you our next question comes from Sarah Parsons. Your line is open.

Sarah Parsons: Hi. And thank you for the presentation. Our company is developing some rather novel technology and software. It's a system and we're rather struggling with the idea that this is a device at all. And I was wondering is a pre-submission the mechanism to bring this to FDA's attention to get advice with what potential regulation it might fall under?

Patrick Antkowiak: Yes, Sarah, thanks for the question. This is Patrick again. Yes, pre-submission is appropriate if you provide your device and description. It's certainly appropriate to ask for whether this is a device for informal feedback.

If you want a formal determination of that you should submit a 513(g) which I believe Kristen referenced in her slides. That would be the formal appropriate way to go about that.

Sarah Parsons: Thank you.

Coordinator: Thank you. Our next question comes from Ana Macheed. Your line is open, ma'am.

Ana Macheed: Hey, thanks for taking the call. And thanks for the webinar. I can only say to the rest of the participants how useful is to approach the FDA very early. I don't think it's ever too early but usually it's very late. So just my experience, I encourage startups to approach the FDA without fear early.

In the last webinar you discussed about the early feasibility studies about collecting small samples of data and approach the FDA. You haven't mentioned much about that in the presentation today. So can you advise new companies and new technologies on how do you couple the early feasibility studies with the consultation process?

Dr. Carlos Pena: Sorry, can you repeat the early feasibility studies program with the consultation process?

Ana Macheed: Yes, with this kind of classification De Novo or pre-submission path. So how do you use the early feasibility study as a way to bring some preliminary data to then submit the De Novo application?

Dr. Carlos Pena: So I can start off (I look to other staff) -- this is Carlos, hi -- the early feasibility study program can be a good place to collect additional information - preliminary safety and effectiveness data about your product. And that may assist in the final marketing authorization decision for your device.

We would probably want to have discussions during the clinical study phase to make sure that the data that you're collecting matches to the expectations that we would want to have before making a decision, when ultimately that device would be made available to patients.

But that's a sort of an iterative process between you know, any clinical study phase and the types of interactions you would want to have via the pre-submission process as you would want to move that product to the market. Does that make sense?

Ana Macheed: Yes, thank you.

Coordinator: Thank you. Our next question comes from Gary. Your line is open, sir.

Gary: Great, thank you for taking my question and thank you all for taking the time to put this webinar together. My question comes back to clarification from the case study on TMS.

And when we look at - I missed what the punch line was relative to the comparison to the ENeuro device as being a predicate and then also the final classification rationale. Was that a class three as a result of being functionally related to the Medtronic Activa?

Kristen Bowsher: Hi, this is Kristen. Yes, one I'd refer you to read through the case study. It's multiple pages and includes a lot more information than I've presented. But I think the final determination was that the ENeuro was not an appropriate predicate device because of the intended device.

And that we thought - it's likely that because the Activa Parkinson's control was an implanted device it has - and a high-risk device, the TMS may be a low to moderate risk once the risk analysis is done and the data's collected.

Gary: Okay. So there wasn't a final determination it could possibly be a class two because it was less invasive or less risk than the...

((Crosstalk))

Kristen Bowsher: Yes, we'd have - that was - they - in the actual case study they are very likely going the De Novo route. But then their next step is to actually collect their clinical data and then once that's collected we can see if any new risks come up that may pop it to a higher risk. But on the surface it looks like a class two De Novo.

Gary: Okay. And just back to the intended use where the Enuera wasn't applicable, is that because of the Parkinsonian...

Kristen Bowsher: Yes, migraine versus Parkinson’s.

Gary: Okay, great, thank you.

Coordinator: Thank you. Our next question comes from Mark McCarty. Your line is open, sir.

Mark McCarty: Hi, thank you for taking another question. This is kind of a broad question. Was the agency's motivation for holding this webinar, just that you've had some problems with De Novo applications for this particular device in the past, or are you trying to reach out a little bit to industry in order to encourage a little bit more participating in development of this kind of device?

Dr. Carlos Pena: Hey Mark, good question. Both sets of questions. I think what we're trying to do is we're trying to make sure -- as this is a up-and-coming emerging technology area -- we're trying to make sure that the regulatory landscape for these products is as transparent and as clear as possible.

And when there is areas of uncertainty -- about how to engage or what is needed -- we're trying to make as many resources available. So it's the latter point that you raise. We're trying to reach out to sponsors and developers to make sure that they have all the tools available to them that we can offer and as moving as expeditiously as possible safe and effective devices to marketplace.

Mark McCarty: All right so you are trying to encourage a little bit more interests on the part of industry in this kind of device then. The reason I ask is because you all did publish that article in Neuro -- which actually is not available it's on a subscription -- but it does kind of seem like you've got a fairly extensive outreach program going here for De Novo devices.

You know, is there sort of a feeling that you know, the PMA pathway is - or I guess I should ask is there a feeling at FDA that many of these devices are legitimately class two and that developers are of the view that they're necessarily class three? Is that sort of the background noise here?

Dr. Carlos Pena: So the - I think you know, a couple comments. One is that we are planning to have a pre-market approval webinar later this year hopefully in the spring summer timeframe. And so I think there we'll dive into that regulatory pathway.

We're trying to sort of hit some of the highlights of medical device development. So September was the IDE, now is the De Novo, next is the pre-market approval. So that's sort of where we're trying to hit across the board.

The broader question that you're asking about the complexity of the De Novo path - you know, the devices that may go down the De Novo pathway versus a PMA pathway, it really depends upon us talking about a specific product and the technology, the indication for use, how it will be used, the prior studies, the precedents of the device. So it's hard for me to sort of answer that specific question about, you know, whether we're...

Mark McCarty: Okay.

Dr. Carlos Pena: ...making a statement about De Novos when we really need to talk about a specific product. And I think the only way we're going to be able to do that is with a submission with a sponsor or developer, innovator.

Mark McCarty: Okay.

Dr. Carlos Pena: But I think the message here that we're trying to get across is that regardless of what product you're talking about we are offering ways for products to move through the process very efficiently.

Mark McCarty: Okay. Yes, the fact that you're having a PMA webinar later this year like kind of answers the question. Thank you very much. I do appreciate it.

Dr. Carlos Pena: Okay, great.

Irene Aihie: We'll take our next question.

Coordinator: Thank you. Our next question comes from James Toyka. Your line is open.

Dave Sonneyka: Dave Sonneyka. I wasn't sure if that was...

Coordinator: Yes, Dave, that's you.

Dave Sonneyka: Thank you. When we were originally looking at submitting our device I was looking at it (unintelligible) which was a very broad (unintelligible). Since that time I wanted to create a sub classification for the trans-cranial - not trans-cranial, sorry trans-cutaneous (neural) stimulators.

One thing that our testing showed though was that more than electrical stimulation it was actually the frequencies of those electrical impulses that had the greatest impact on the test subjects. And that changed the whole scope of the development of the product and the range of conditions or indications for which it would be used.

And it seems that most FDA devices are indicated for a specific condition whereas the device that we're developing, preparing, testing, is really focused

at a much broader range with (unintelligible) frequencies for different conditions or symptoms.

How does that fit into this scheme of things? Do we have to have device for every one or is there a broader classification for those kinds of things?

Michael Hoffmann: Hello, this is Michael Hoffmann. In general I - well I would say that typically there's one indication for a device and we would be looking at evidence to support that indication. So as far as a general (unintelligible) I'm not - I think that's something that we'd have to - something that would actually be a really good topic for a pre-submission.

Especially if you have some information that you'd like to discuss about your product and how you're looking to market it. Especially if there's potentially multiple pathways or multiple indications that you're looking at.

Dave Sonneyka: Okay. And that's certainly what we would like our studies to be. And so look to putting together a pre-submission and addressing that on this sooner.

We've been at this process for about eight years now of studies and have been waiting for an opportunity and the De Novo process changes a couple years ago seemed to make this a much more desirable time to approach the FDA. So we will proceed with that, thank you.

Irene Aihie: We'll take our next question.

Coordinator: Nativa Bradshaw, your line is open.

Nativa Bradshaw: Hello, thank you for taking my call. Yes, my question was about classification of devices. I understand that (it's) useful to look for a predicate when it comes to getting a 510(k) approval and clearance of your device.

And if you already have a device that you have your eye on for predicate that's actually already classified as a class three, can you just use that as a predicate for 510(k) or is it necessary that you always go through a PMA for classification of a class three device?

Michael Hoffmann: Sorry can you repeat that question? Just - I think just so we can have clarification on what the question is?

Nativa Bradshaw: Yes. What I basically wanted to know is can a class three device be used as a predicate for a 510(k) submission?

Michael Hoffmann: If it's a - or a class three device that's a PMA device?

Nativa Bradshaw: Yes, that was actually approved via PMA. But is it possible that it can be used as a predicate towards doing a 510(k) submission? Since the PMA was already approved for the device.

Michael Hoffmann: If the PMA is approved then if your device is most similar to that device it's quite likely that that would be a PMA device. But it would not be an appropriate comparator for your 510(k) device. Again, a pre-submission if there's - maybe there's some specifics that would be worth discussing if you'd want to submit a pre-submission but that generally is how we would review that.

Kristen Bowsher: Yes, I would just mention that if the PMA - if you thought the PMA should be reclassified into an a class two device which could be used as a predicate - a reclassification petition could be submitted.

Nativa Bradshaw: Excellent, that's exactly what I thought. Thank you so much.

Irene Aihie: We'll take our next question. Operator, are you there?

Watson: Hello?

Coordinator: Mr. Swanson your line is open.

Watson: Hello, thank you for the presentation and thank you for taking my call. This is probably a straightforward question, a straightforward answer, so hopefully it's an easy one but you've used the phrase sponsors developers and innovators several times. Can I get a broad, basic definition of the three?

Dr. Carlos Pena: Medical device developers.

Kristen Bowsher: Generally when we're speaking internally people who have submitted submissions to us may be referred to as sponsors. But they can also - they're probably medical device innovators as well but it's kind of the lingo we use.

Dr. Carlos Pena: Yes, it's meant to capture a lot of different populations. And sometimes we may use different terms to make sure that we're reaching out to as broad a group as possible.

Swanson: So all three can be a manufacturer, right? But or maybe approaching a treatment solution or an efficacy solution from different angles?

Dr. Carlos Pena: Either different angles or different environments. Some can be from academia, some can be from industry, some can be from other government agencies, you know, it's sort of meant to describe a lot of different people that are interested in developing the technology.

Swanson: Thank you very much.

Coordinator: I am showing no further questions in the queue.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions. Today's presentation and transcript will be made available on the CDRH Learn webpage at www.fda.gov/training/CDRHLearn by Thursday, March 30.

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 the live presentation. Again, thank you for participating. This concludes today's webinar.

Coordinator: Thank you all for participating in today's conference. You may disconnect your line and have a great day or a great evening.

END