NWX-HHS FDA (US)

Moderator: Irene Aihie
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Coordinator: 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 please disconnect at this time. I would like now like to turn the meeting over to your host Ms. Irene Aihie. You may begin.

Irene Aihie: Hello and welcome to today's FDA Webinar. I am Irene Aihie of CDRH's Office of Communications and Education. Today we will be discussing the final guidance document FDA Decisions for Investigational Device Exemption, IDE, Clinical Investigations which was published on August 18, 2014.

The final guidance described the FDA's decision making and communications regarding applications from companies that want to conduct medical device clinical trials in the US. It also described more flexible options for clinical study approval that allow clinical studies to begin sooner while ensuring patient protection.

Today Owen Faris Acting Clinical Trial Director and CDRH's Office of Device Evaluation will present an overview of the guidance document including what has changed from draft to final. And will answer questions following the presentation.

Also with us today to assist the Q&A portion of our Webinar are other subject matter experts from the Office of Device Evaluation, and Office of Communication and Education.

We have become aware of a typo in the original email announcement and guidance and webinar. We apologize for this error. If you are having difficulty logging in to the Web portion of today's webinar, you can log in with the link and conference number available in the email.

However, please use pass code 1405152. Additionally the slide presentation is available on the CDRH Learn section of the FDA Web site at fda.gov/training/cbrhlearn under the heading How to Market your Device.

Following the webinar the audio recording and written transcript of today's program will be available on the CDRH Learn. Now I give you Owen.

Owen Faris: Good afternoon. My name is Owen Faris and I'm the Acting Clinical Trials Director in the Center for Devices and Radiological Health. And I was also the lead author on the first two drafts of this guidance as well as the final guidance.

So let me just start with an overview of what we're going to discuss today. First we're going to talk a little bit about what this is all about and how this guidance fits into our FDA strategic priority.

I'm going to define what a guidance document means very briefly and define what an investigational device exemption study is. I'm going to talk a little bit about the history and the original goals of this guidance because there is quite a lengthy history to this guidance.

I'm going to talk a little bit about some changes in the law that occurred during the writing and draft period of this guidance that impacted what we have in our final document. I'm going to talk about what has changed in the final document compared to the draft guidance.

And then I'm going to walk through some of the meat of the guidance itself. In particular the decisions that we make for different IDEs and some of the bases of those decisions. And then I'm going to close with talking about how we communicate our decisions in our letters.

So first our strategic priorities. So CBRH has identified a strategic priority, the goal of improving US patient access to new devices by strengthening and streamlining the clinical trial enterprise so that medical device clinical trials are conducted in the US in efficient cost effective manner while maintaining appropriate patient protections.

So this guidance really fits into that in that it introduces processes that allow a more efficient study enrollments to reduce the time and cost associated with the conduct of clinical trials. Provides information regarding our decision making process in order to improve predictability of the regulatory process.

And it introduces communications intended to improve the transparency of FDA's decision making process to study sponsors and other stakeholders.

So what is a guidance document? A guidance document explains our current thinking on a topic. But it's important to note that it doesn't establish legally enforceable responsibilities. And what we say in that document really should be viewed as recommendations unless there are specific regulatory or statutory requirements cited.

So what is an IDE or an Investigational Device Exemption? It's established in Section 520 of the FD&C Act. An FDA approval of an IDE is required for US human study of a significant risk device which is not improved or cleared for the indication being study.

It exempts sponsors from certain provisions of the FD&C Act. For example requirement of a marketing application and compliance with full GMPs. There are requirements for informed consent, labeling, monitoring of the study and records and reporting. And initiation of the study also requires approval by an institutional review board or IRB.

So as I mentioned this guidance has quite a lengthy history. It was originally published on November 10 of 2011 and explained each of the possible FDA decisions that we can make when reviewing an IDE.

Those would be approval, approval with conditions, and disapproval. And it provides examples of reasons that could support IDE disapproval or approval with conditions. And it also explained a new mechanism that we termed stage approval which allows some studies to begin while issues are addressed concurrently.

However during the draft period of that guidance, actually shortly following the closure of the comment period for that first draft, the law was changed

under FDASIA 601. Section 601 amends 520G Part 4 Part C of the FD&C Act and became law in July 9 of 2012.

And specifically there was an element of that that targeted some elements that were somewhat inconsistent with the current draft of the guidance. And I'll reference the specific language which was FDA shall not disapprove an IDE because the investigation may not support a substantial equivalence or de novo classification determination, or approval of a device.

The investigation may not meet a requirement including a data requirement relating to the approval or clearance of a device. Or an additional or a different investigation may be necessary to support clearance or approval of a device.

So what does that mean? That essentially means that an IDE cannot be disapproved on the basis of FDA's belief that the study design is inadequate to support a future PMA, 510K, HDE, or de novo classification.

Of note the standards for market approval or clearance of a 510K did not change under FDASIA.

So once that law changed FDA and CDRH in particular had to sort of spend a little time thinking about how we were going to modify our guidance to be consistent with the changes to the law.

So we formed a working group that developed some policies around IDE decision making. We made modifications to our IDE decision letters that would be consistent with the new requirements under the law. We considered other mechanisms to encourage sponsors to work with FDA to develop pivotal trials that were appropriately designed to support marketing applications.

So the thinking being that we were no longer in a position to disapprove those studies if they were adequately protecting subjects. But we and other stakeholders and sponsors still have an interest in developing the right study to support future marketing applications.

So we were exploring ways to do that in an appropriate way that would be consistent with the law.

We re-issued guidance for public comment in June of 2013. That closed in September of 2013. We received a lot of very good comments. And based on those comments and our considerations of those comments we made some modifications that I'm about to discuss in issuing the final guidance.

So first off I'll start with what is nearly unchanged from the draft guidance. So our explanation for the reasons for which FDA may disapprove an IDE was not substantially changed.

Our explanation for the mechanisms of approving an IDE was not substantially changed. So approval, approval with conditions were nearly identical between the most recent draft and our current final document.

We did make some minor modifications to our explanation of staged approval. They were mainly for clarification. And I'm going to walk through all of these mechanisms in the next few slides.

So what did change from the most recent draft to the final document? We did change how study design considerations and future considerations will be communicated to sponsors. And I'm going to explain that.

And we removed a proposal that we had put in the most recent draft, a new voluntary comprehensive, interactive review process to assist sponsors in development of appropriately designed pivotal studies. We termed that process the pre-decisional IDE. And based on the comments we decided to remove that. And I will explain why in the preceding slides.

So let's dig into the meat a little bit of what this guidance has to offer. So I'll start by talking about what are the three main decisions that FDA can render when an IDE is reviewed by CDRH.

So there is approval. And that can be approval of the full study cohort or staged approval. And I'll explain what that means. There is approval with conditions. And that, again, can be approval of the full study cohort or staged approval. And then there's disapproval. And we're going to walk through each of those.

So first off let's talk about approval. FDA approval, also called full approval, means that we don't have any remaining questions that must be addressed prior to enrollment of the approved number of subjects.

The study's approved for a specified number of subjects and investigational centers. And the study can be initiated upon IRB approval. Our letter wouldn't convey any outstanding questions that need to be addressed in order for the study to move forward.

So that was the easy one. Now we'll start getting into the more complicated ones. So approval with conditions. Approval with conditions means that FDA has determined that despite some outstanding issues the information provided is sufficient to justify human clinical evaluation of the device. And the

proposed study design is acceptable with regard to protection of study of subjects.

Resolution of the outstanding issues isn't required prior to the initiation of enrollment in the study with exception of certain issues related to the influence and consent which must be corrected prior to enrollment.

And the sponsor can begin the study upon receipt of IRB approval on the condition that within 45 days from the date of FDA's decision letter the sponsor submits information addressing the issues identified in FDA's letter.

So let's talk about some of the examples of typical conditions that might be conveyed in an approval with conditions letters. Requests for additional information, data or changes that relate to protecting subjects in the study and can be addressed in a timely manner, 45 days but for which FDA determines that they do not need to be resolved prior to study initiation.

Late stage follow-up procedures and assessments that relate to the care of study subjects but because they occur late in the study they'll likely be addressed prior to subjects reaching that point in the study. And minor issues relating to the informed consent document that must be corrected before study initiation but can be reviewed by FDA after initiation.

Let's talk about staged approval because that can apply both to approval or approval with conditions. And it's granted while certain outstanding questions are answered concurrently with the enrolment of a limited number of subjects.

So the thinking here is that if the benefit risk profile is sufficiently favorable to justify an enrollment of a portion of the study subjects, a staged clinical investigation allows initiation of the study that might otherwise be

disapproved while providing additional mitigation of risk by limiting exposure of the device to a smaller subject population.

The sponsor will be permitted to expand enrollment once an IDE supplement containing the necessary additional information is submitted to FDA and found to be acceptable.

So let me just go into a little bit of detail of how that might play out. We might receive an IDE application where the sponsor is asking for enrollment of say 300 subjects. And we may have some outstanding questions that will be answered during the course of the early stages of enrollment of that study either from external information, non-clinical information that can be gathered concurrently, or from the clinical information being gathered early in that study.

And we may not at this point feel comfortable exposing all 300 subjects but we may feel like there is a reasonable profile in terms of benefits and risks for subjects that it is reasonable to allow a limited exposure for say, 30 subjects.

And we might allow those 30 subjects to be enrolled while the additional information is being gathered. And when that information is gathered the sponsor could come to FDA and with an IDE supplement providing that information and request expansion of that study.

The staged approval might be appropriate when additional clinical information confirmation of the safety profile, the potential for benefit is obtained by reviewing initial data from subjects enrolled early in the clinical investigation before enrolling the entire subject cohort.

Or when additional confirmatory non-clinical testing is needed to more fully characterize the device performance to adequately evaluate the potential for risk of the device before permitting the entire subject cohorts and it's conducted concurrently with early enrollment in the clinical investigation.

Now we can do staged approval with essentially any kind of study. But we frankly see this more commonly with pivotal studies where the device design is finalized. We know enough to design the study itself but we have some outstanding question that needs to be answered before the entire cohort is exposed to risk of the device in the study.

And there are some specific considerations for pivotal studies that are noted in the guidance that I'll walk through now. So when staged approval is applied to a pivotal study it's important to understand that successful support of a marketing application under staged approval really isn't expected until the full plan cohort is subject is studied.

Also a staged pivotal study really should only be considered if the additional information that's requested isn't expected to result in changes to important elements of the clinical investigations such as endpoints, sample size, stopping rules, or to the device design.

If we're still at the stage where we don't know fully how to design the clinical study or we haven't finalized the device design we're probably not ready for a pivotal study at that point. And probably a feasibility study is more appropriate than a staged pivotal.

Some additional considerations for pivotal studies. At the end we determine that a new feasibility - that new feasibility data are really needed prior to approval of the proposed pivotal study in order to allow for a more

comprehensive examination of the study outcomes related to device safety in a small number of subjects prior to exposing a large group of subjects to the study.

So my point here is that staged approval really works best when there is a single specific question that can be answered in a concise manner. If we don't know enough to formulate that question and we really have a broad set of questions around the safety of the device that need to be answered in the smaller cohort of subjects.

Again that probably isn't the time for a staged pivotal study. We're probably talking about a feasibility study that can be more comprehensively examined.

The data requested by FDA also shouldn't inappropriately un-blind any of the relevant stakeholders including the sponsor, investigators, study management personnel, to critical study data.

So most of the time we're talking about data that are not directly related to the primary outcomes of the study. So we might have a particular safety question about certain adverse event rates associated with the implant procedure of the device or something along those lines.

But typically we're not asking for the outcome data that will be the primary endpoint of the study. And we're not asking for data that is so directly related to that that presentation of that data, knowledge of that data, would taint the quality of the data and start to lead to questions of data integrity.

So let's move on to disapproval. So disapproval essentially means that the sponsor may not initiate the clinical investigation until the sponsor submits an amendment to the IDE to respond to the deficiencies identified in FDA's letter

and subsequently receives a new letter from FDA granting approval or approval with conditions.

So again I'll remind you that FDASIA changed to a certain extent the criteria by which we might disapprove a study. And that was cause for the second draft of the guidance. But I will remind you also that the standards for protection for study subjects remain unchanged.

So issues regarding protection of subject whether they be related to study design or non-clinical testing still remain reasons for disapproval. And I'm going to go into some of the specifics of where we might fall out on that.

Also per FDASIA issues regarding the study design that are not related to protecting study subjects are not the basis for disapproval or an approval with conditions decision. And instead they would be conveyed as study design considerations. And I'm going to explain what that means as well.

So I'm going to go through some of the reasons that are associated in the regulations for disapproval. And I'm going to explain a little bit about what we think that means in terms of practical consequences.

So consistent with 24 CFR 812 Part 30B and Section 520G of the FD&C Act, FDA may disapprove an IDE for any of the following reasons. There has been a failure to comply with any requirements and 21 CFR Part 812 or 520G of the FD&C Act. Any other applicable regulation or statute or any condition of approval imposed by an IRB or FDA.

The application or report contains an untrue statement of material fact or omits material information required by a 21 CFR Part 812. The sponsor fails

to respond to a request for additional information within the time prescribed by FDA.

There is reason to believe that the risks to subjects are not outweighed by the anticipated benefits to subjects and the importance of the knowledge to be gained. So that really speaks to, you know, as the investigational plan adequately protecting study subjects.

Is it exposing the subjects to unacceptable probable risks? Or does it fail to adequately protect study subjects from probably risks?

Another reason, the informed consent requires changes to adequately inform subjects of the study and must be reviewed by FDA prior to study initiation. So you'll note that I also talked about informed consent being a reason for approval with conditions decision which is very commonly the case.

If the informed consent has some essentially some very clear cut issues that we believe can be addressed by the sponsor prior to our review and implemented then that would typically be a reason for approval with conditions.

But if the informed consent contains an element that we are concerned about that we believe is so essential that we must review it prior to subjects being enrolled in that study then that would be a basis for disapproval.

The investigation as proposed is scientifically unsound because it does not pose a reasonable scientific question or the investigation does not include collection of data or information related to that scientific question.

So I will point out that scientifically unsound doesn't include concerns that the study design will not support a marketing application.

There is reason to believe that the device as used is ineffective. So here we're talking about inadequate potential for benefit so the available data suggests the device is ineffective or no information has been provided to suggest the device as used may result in patient benefit and the generation of knowledge adequate to justify the risks.

It is otherwise unreasonable to begin or to continue the investigation only to the way in which the device is used or the adequacy of the report of prior investigations or the investigational plan, the methods, facilities, and controls used for the manufacturing, processing, packaging, storage, and where appropriate installation of the device or monitoring or reviewing the investigation.

So in large part we're talking about device safety here, the data and information provided are insufficient to adequately characterize a safety profile of the device such that human clinical investigation is not considered reasonable.

So the guidance goes into a little bit more detail and there are some examples of some of the reasons why we might disapprove the study.

So I'd like to talk a little bit about study design considerations. This is a mechanism that we implemented after the first draft of the guidance following the changes in the law. As a mechanism by which we could provide recommendations to a sponsor regarding changes that we believe should be made in order for the study to support its primary goals but that were not the basis for disapproval or an approval with conditions decision.

So examples of those kinds of considerations include issues related to primary and secondary, major secondary endpoints, randomization control and blinding, follow-up duration in assessments, statistical analysis plans, and enrollment criteria if not related to subject protection.

And I'll just emphasize that anything that is related to subject protection even if it deals with study design may still be a basis for a deficiency. The bar for protecting subjects is not changed.

So what are future considerations? So future considerations have been around for a long time but are also an important element that we described in the guidance. Future considerations are intended to provide helpful advice to sponsors regarding important elements of the future application of the IDE may not specifically address.

So some examples. Known limitations of the IDE clinical investigation with regard to supporting certain claims or indications. Specific non-clinical testing that while not necessary to support approval of the IDE would be needed to support the marketing application.

So here we're going to get into some of the changes that we have implemented in the guidance most recently. So the draft guidance proposed that study design considerations be included in the section of the IDE decision letter itself.

We specifically requested comment on that proposal and we received quite a few. So FDA received comments from several stakeholders that proposed that FDA provide study design considerations and FDA's assessment of the study design as a separate communication and not in an IDE decision letter itself.

However some other stakeholders expressed support for inclusion of the study design considerations in the letter. And others really didn't discuss where the study design considerations go. But they did focus on ensuring that they decision letter clearly conveys whether or not FDA believes that the study design is adequate to support goals.

So based on the comments received FDA believes that when study design considerations are included in the body of a decision letter there is the potential for study design considerations to be misinterpreted by sponsors and other stakeholders as issues that are required to be addressed rather than as recommendations.

Therefore FDA intends to convey study design considerations in a separate attachment included with the decision letter rather than in the body of the letter. And the decision letter itself will state whether FDA believes that the study design is adequate to support the study goals or whether FDA recommends study design considerations in order for the study to do so.

And if we do recommend study design considerations our letter will note the following. These recommendations do not relate to the safety, rights, or welfare of study subjects. And they do not need to be addressed in order for you to conduct your study.

So essentially we're trying to make sure that everyone, all stakeholders involved in reading this letter and making decisions related to this letter understand our intention here which is to convey elements that we believe are important.

And we strongly believe the sponsor should address to support the study being as meaningful as possible and as useful as possible in the future iterations of this device.

We think that it's very important to have the sponsor be fully informed of the extent of FDA's review. And be able to consider these recommendations so that whatever is next whether that be a future pivotal study if this is a feasibility study.

Or whether that be a future marketing application that the sponsor is as well informed as possible about how to move a potentially important technology forward. And such that the study itself is ideally designed to be, to make the most of the information gathered and be as useful and meaningful as possible.

So I also note that we will continue to engage with stakeholders on this issue and make modifications to approach them in the future depending on our experience thus far.

So similarly with future considerations we received comments proposing that the agency provide future considerations as a separate communication not in the decision letter. And we think there are good reasons for this as well.

So based on the comments received we intend to convey the future considerations as a separate attachment similarly to design considerations. And that attachment will again be included with the decision letter rather than in the body of the letter itself.

So I'm going to briefly touch on a proposal that is not in this final guidance. The most recent draft of the guidance proposed a new mechanism for review and interaction for pivotal IDEs.

We called this the pre-decisional IDE. This process was comprehensive FDA review of a draft IDE prior to formal IDE submission, followed by written feedback from FDA in an interactive discussion between FDA and the sponsor.

And the goal of the pre-decisional IDE was to facilitate the development of an approved IDE submission that would be more likely to be approved and include a study design that would be adequate to support a future marketing application. This was focused on pivotal studies.

However FDA received relatively mixed comments. We received several comments expressing concern that the pre-decisional IDE process itself might be too time consuming or require extensive FDA resources that could be better allocated elsewhere.

And upon further consideration we also believe that our pre-submission process which is a very active and meaningful process can address many of the same goals. And so based on the comments received and FDA's considerations of the points raised, FDA will not pursue the pre-decisional IDE at this time.

I provided a link for the guidance. And I think that is probably my last slide. I think we are ready for questions.

Coordinator: Thank you. And we will now begin the question and answer session. If you would like to ask a question please press star 1 and record your first and last name clearly when prompted.

Your name is required to introduce your question. To withdraw your question you may press star 2. Once again if you would like to ask a question please press star 1. One moment please for our first question.

Our first question is from (Amy Harold). Your line is open.

(Amy Harold): My question is what constitutes a feasibility study versus a staged pivotal study? And is there a difference in the FDA review processes for these two different studies?

Owen Faris: So that's a great question. So first off I'll take the second part of your question first. There aren't any differences in the review process. From a time prospective all IDEs are reviewed within 30 days.

We have a similar team that would review either a feasibility or a pivotal study. And so from a review process and the decisions that we can make in all of that there really aren't any fundamental differences.

But I think there are differences in terms of what the intent of that study is. And so I think there are times when, there, when you have a device design that is essentially final. And you know enough to design your pivotal study.

But you - there may be some outstanding questions that we believe and potentially the sponsor believes as well should be answered before the entire pivotal study cohort is exposed to the risks of the device in the study.

And that's the perfect time to do a staged pivotal study where there is a discreet question being asked that might be a non-clinical question. So it could be the case that in one area of non-clinical testing you've done almost

everything that needs to be done to support the pivotal study. But there's one element or two elements that haven't quite been completed.

Maybe they're going to take three or four months to be completed. We have a lot of other information that is very encouraging with regard to that missing element. So we feel relatively comfortable in that area. And we say okay. You can start your study. But you need to finish up this area of non-clinical testing before the entire study cohort is exposed.

Essentially we are asking for the confirmation of what we believe is already a relatively positive safety profile in that regard. And that's done concurrently with the study moving forward.

It might also be the case that we are asking for something that is internal to the study. So we want to see how the first 30 patients perform with regard to some particular adverse event before we feel comfortable moving forward.

The only way we're going to get that is by starting to have patients be enrolled. But if we know enough about how to design that study there isn't necessarily a reason to force that to be its own feasibility study.

So let me contrast that with what might be more appropriate with the feasibility study. So in a feasibility study we think that, you know, we're in an earlier stage. We probably don't know enough to design every element of that pivotal study. So something is likely to change at the end of that study that is meaningful. Or there's potential for something to change.

So maybe something's going to change within the device itself. And in which case it's time for a feasibility study so that we can open that entire, that data

set entirely up at the end of the day and understand it better. Both the sponsor and FDA to inform that future design.

It's also possible that in many cases the device design is finalized but the study design - so that pivotal study isn't. So we might not know enough to design the appropriate primary endpoint for safety or for effectiveness. Or how best to treat patients in certain elements of use of the device. And we're going to learn that during that feasibility study.

And it wouldn't be appropriate to learn that during the feasibility study and then have those same feasibility study patients part of a pivotal data set. So that's sort of the contrast to a staged pivotal study.

If you need to learn something from the feasibility in order to inform either the device design or something about the testing for that device that we don't fully know. Or something about the clinical trial itself, the design of that study then you probably need to have a feasibility study that informs that. That we can open up entirely and explore before moving forward.

If there is just a single specific question that is not limiting in terms of the design of the device or the study itself, then in some circumstances it's appropriate to ask that single specific question concurrently with early enrollment in the study if we believe that subjects are adequately protected based on everything we know.

Coordinator: Our next question is from (Cathy McNeil). Your line is open.

(Cathy McNeil): Hi. Could you repeat the Web site where we can obtain copies of the slides?

Owen Faris: Just one moment.

Irene Aihie: Yes. You can find it on the CDRH Learn Section of FDA's Web site.

(Cathy McNeil): Thank you.

Irene Aihie: And you'll find it under How to Market your Device.

Coordinator: Our next question is from (Lee Aires). Your line is open.

(Lee Aires): Hi. My name is (Lee Aires) from Oxford Performance Materials. I have a question regarding the pre-IDE review process. I understood from your presentation that it's no longer available. Or did I understand that correctly or incorrectly?

Owen Faris: So you did misunderstand to a certain extent. And I'm glad you asked the question because maybe others misunderstood as well. So I didn't use the term pre-IDE. We've changed that name.

And we no longer use the term pre-IDE because it applies more broadly than just to IDEs. Pre-IDE is part of our Q-submission process. We now call the pre-IDE pre-submission instead.

And it applies to other types of files other than just IDEs. So now that will be termed a pre-submission. So that is alive and well. And we very much encourage sponsors to utilize the pre-submission process.

The term that I used is pre-decisional IDE which was something that we developed as a concept and articulated in the most recent draft and have decided not to implement. But the pre-IDE - formerly known as pre-IDE process, now the pre-submission process is alive and well and (unintelligible).

(Lee Aires): So that means if we were developing a protocol for an IDE we could use the pre-submission process for that?

Owen Faris: Absolutely. We strongly encourage that.

(Lee Aires): Okay.

Owen Faris: Thank you for the question.

(Lee Aires): Thank you. Thank you very much.

Coordinator: Our next question is from (Ken Lupe). Your line is open.

(Ken Lupe): Yes. When is the class of a device determined? And are all IDEs automatically a class three device?

Owen Faris: I think I'm going to defer this question to (Soma Kalb) who's our IDE Director.

(Soma Kalb): Hello. So the class of the device can be determined through a few different mechanisms. We can discuss that during the pre-submission process and through the pre-submissions process.

There's also a formal process called the 513G Process and there's information - there's a guidance about the 513G Process. And there's also a guidance about the pre-submission process as well that's available.

Not all studies requiring IDEs are class three devices. Significant risk studies are those that require IDEs and that considers not only the risk of the device but the risk that might be introduced by the study itself.

If you are unsure about whether your device or study requires an IDE you can submit a, what's called a study risk determination submission. And that is also outlined in our guidance document called pre-submission and meetings with FDA.

So basically that's the answer to the question.

Owen Faris: And I'll just - just follow up with that by saying that, you know, we do even have some class three devices for which the proposed study we determined it is a non-significant risk study and there's no IDE required.

(Ken Lupe): Thank you.

Coordinator: Our next question is from (Velotte). Your line is open.

(Velotte): Hello. I'm (Velotte Unintelligible). And the question I have, patient enrollment protocol and consent approval by IRB. Also protocol amendment approval by IRB for a follow-up change in assessment, followed by another amendment for changing endpoint.

So the question here is that if the protocol is approved and the consent is approved by the IRB, one can patient enrollment begin? Because the second amendment affects the follow-up assessment and at that point it will have an amendment protocol approved by IRB and a consent form.

And the patient will be consented before the assessment is done. And can all these patients that are enrolled before the amendment approval, can they be included as, into the patient population?

Owen Faris: So I'm going to suggest - this sounds like a very specific question that I'm happy to follow-up with you offline. And so I'm going to suggest that you email me at the email address that's on the last slide. And either Soma or I will be happy to work with you on the specifics of the question.

(Velotte): Wonderful. Thank you.

Coordinator: Our next question is from (Argie). Your line is open. And participant your line is open. If your line is muted you can press star 6 to un-mute your line. Again your line is open. We'll go to our next participant. This participant was not able to mention their name. But participant your line is open.

Man: Hi this is (Unintelligible). Can you hear me?

Owen Faris: Yes.

Man: Hi. The question is, when you do IDE approvals they're assigned a Category A or Category B. Now I understand that Category A is by definition an experimental device, while Category B there is some understanding of the safety risk associated with the device.

By categorizing a device as Category A are you automatically implying that they will have post-approval study requirement when a PMA submitted after the fact?

Owen Faris: No...

Man: There is no pre-decision based on post-approval requirement on a Category A device?

Owen Faris: No. We may or may not have post-approval requirements for either a Category A or a Category B device. And that is something that can be discussed during the pre-submission process.

And often we have a pretty good idea as to whether we're likely to require post-approval requirements. But it's essentially unrelated to that designation.

Man: Great. Thank you.

Irene Aihie: We'll go ahead and take the next question. Operator are you there? Operator are you there? Unfortunately we're having some technical difficulties. So as a reminder if you have any questions please email your questions to DICE, that's D-I-C-E @fda.hhs.gov.

We do apologize for the technical difficulties. Thank you. This is Irene Aihie again. We appreciate and thank you for your participation in today's webinar. Again we apologize for the technical difficulty.

Please remember that this presentation will be available on the CDRH Learning Section of fda.gov. The written transcript will take a couple of days but should be posted no later than Wednesday, September 10th.

If you have any additional questions please use the contact information provided at the end of the slide presentation. As always we appreciate your feedback on today's presentation. Again thank you for participating and this concludes today's webinar.

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