NWX-HHS FDA (US)

Moderator: Irene Aihie
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Coordinator: Thank you for standing by. At this time, all participants are in a listen-only mode. After the presentation, we'll conduct a question and answer session. To ask a question, please press the star 1 and please record your name. Questions will only be taken by phone and not through the chat on the net.

Today's conference is being recorded. If you have any objections, you may disconnect at this time. I would like to introduce your host for today's conference, 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 Communication and Education. CDRH strives to ensure that patients in the U.S. have access to high-quality, safe, and effective medical devices.

To meet this challenge, the Center's Medical Device Clinical Trials Program has been changing and improving. Some of these changes include the issuing of guidance documents and revising our organizational structure and policies.

Although we've communicated these changes individually, today's webinar will provide the opportunity to learn about the current state of the program

and discuss some recent modifications, outlining where we are now and where we are going.

Owen Faris, Acting Clinical Trials Director in CDRH's Office of Device Evaluation, will be our presenter today. Owen's presentation will include the clinical trials priority, IDE SOP implementation, our performance in fiscal year 2014, our goals for performance in fiscal year 2015, early feasibility studies, and future program plans.

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

Please help us continue to improve our communications and outreach about the Medical Device Clinical Trials Program by completing the online survey that Owen will reference throughout his presentation. Now, I give you Owen.

Owen Faris: Good afternoon. My name is Owen Faris, and I'm the Acting Clinical Trials Director in the Office of Device Evaluation in the Center for Devices and Radiological Health. And today I'm going to talk to you about our efforts directed towards strengthening the medical device clinical trial enterprise.

But before I really get started with my talk, I'm going to start, actually, with a little bit of a plea for all of you. So as you're going to hear today, we've been doing quite a lot in the area of medical device clinical trials. We're very excited about what we've accomplished so far and what's still in front of us to accomplish.

But we also recognize that making future progress is really going to depend on, to a great deal, on our interaction and efforts for outreach with our external stakeholders.

And so we're really asking you to help us with that and figure out what best works for you, what your needs are, and what format is most useful for you in receiving guidance and information from FDA with regard to medical device clinical trials.

We have a team of folks that are really interested in seeing the results from this short survey, and we're hoping that you can really help us by giving some information. We expect that this survey will take five minutes or less, and I'm showing the link here.

I'm also going to show it at the bottom of most of my slides today, and I'll show it at the very end as well. And just, please, if you have the time to give us some information that will help guide us, that would be very helpful.

So now, on to the talk. So today I'm going to talk a bit about, very quickly, about our overall strategic priorities for 2014 and '15. Then I'm going to focus on the clinical trial enterprise priority. I'm going to talk about what we've done over the past year and what results we've seen, as well as where we think we can go in the future.

I'm going to give a special focus to early feasibility studies, and then talk about some additional future plans and some ideas for that. And I should mention, as Irene said, that we have several experts from throughout the Center in the room here with me that are going to be really helpful with answering some of the questions that you may have at the end of the talk.

So I'm not going to talk in a lot of detail about the three strategic priorities that we have for 2014 and 2015, just to note that they are: One, strengthening the clinical trial enterprise; two, striking the right balance between premarket and postmarket data collection; and three, providing excellent customer service.

And I think you can see that the three of these, in combination, really reflect a holistic view of CDRH's efforts to bring important medical devices to U.S. patients as quickly and efficiently as possible. And so the rest of my talk today is really going to focus on this top priority of strengthening the clinical trial enterprise.

So as most of you probably know, our Investigational Device Exemption, or IDE, is a process by which sponsors of clinical studies for medical devices request and receive approval to conduct those studies, either for devices that are not approved or are approved for a different indication than for which the study is being proposed to evaluate.

And so this is a process that's very important to the clinical trial enterprise, and it's really the process where FDA has the most influence in improving the efficiency and effectiveness of that process.

So we defined two goals in this area. The first, to improve the efficiency, consistency, and predictability of the IDE process; to reduce the time and number of cycles needed to reach appropriate IDE full approval for medical devices in general, and for devices of public health importance in particular.

So let me just pause there for a moment and talk a little bit about what we mean there. So any time an IDE is submitted to FDA, we review it within 30 days. But many studies take more than one review cycle and quite a few rounds of going back and forth between FDA and the sponsor before we reach

a point where we can fully approve that study and that device study can move forward.

Our second goal is to increase the number of early feasibility, first in human studies submitted to FDA and conducted in the U.S. And I'm going to go into that in great detail in the preceding slides.

So let's talk about what the IDE challenge is. So I think that many of us recognize that the IDE review process is really a very important part of protecting subjects in investigational device studies.

It's the process by which FDA makes sure that there's a demonstration of safety and potential for effectiveness that justifies the risks that subjects will be exposed to in taking part in that study, and it's really our place to make sure that we are adequately protecting subjects.

We also recognize that sooner is better when it's an appropriate approval. So the sooner an IDE is approved, the sooner that a potentially important technology can be made available to you as subjects, and that, that study can eventually lead, potentially, to a market approval of a device if it's shown to be both safe and effective.

And in looking at that process, we recognize that there have been times historically, and there continue, frankly, to be times today where there are what I will call avoidable bottlenecks in that process - areas where the efficiency could be improved.

We could be improving the way in which we make a decision or communicate that decision, such that we move to an appropriate full approval more quickly and that study can proceed.

So recognizing that, all of our efforts this past year that I'm going to talk about today are really looking at an acknowledgement that we can and should look for ways to improve that process for FDA's decision making and looking at the best ways to implement those changes.

So what are doing to achieve that? So we've had quite a bit of work in the past year-and-a-half or so do develop a clinical trials program. We developed that position of Clinical Trials Director, of which I'm acting, in February of 2014. So the better part of a year now, we've been operating under that model.

And one of the important elements of that program was to establish an SOP, that I'm going to walk through in detail, for how the Clinical Trials Director will be involved in the review of certain IDE decisions.

And I think these three sub-bullets here are really key for describing how we're approaching this issue. So the first really being ensuring that CDRH is in the right place. So we have a very energetic staff that is very interested in reviewing these clinical trials, very excited about these innovative devices that can more forward and play a role in medical treatments for patients.

That said, it's very easy when we're looking at a complicated submission to come up with a lot of reasons for why we might say no, in terms of nonclinical testing that maybe leaves some uncertainty, some questions not fully resolved; in terms of elements of the clinical trial protocol that, potentially, could be modified or something could be added to it that might add some protections for patients.

And these are all very important questions to be thinking about and potentially raising in our decision. That said, we have to balance that with an

understanding that we never have complete certainty about many of the issues that are in question when we're making an IDE decision.

And that we have to balance our desire to ask questions to reduce that certainty with an understanding that we also have a duty to promote important medical technologies for our patients, and that the right place reflects a balance of asking questions that protect patients, but also recognizing that we have a role in accepting some level of uncertainty to appropriately move technologies forward.

And that's a really difficult place to strike the right balance, and that's an area where we believe that some additional oversight is helpful. So second bullet, which is very much related to that, is ensuring that we're applying flexibility where appropriate.

So that means that in certain instances we might say that, given the state of study, we're not going to ask for complete testing in a certain arear prior to moving on to that next stage. So we might ask for a certain level of, say, mechanical testing at the feasibility study stage, and then more complete mechanical testing prior to that pivotal study.

Those are the sorts of things where we're trying to think about where can we be flexible, such that we're striking the right balance in moving technologies forward while protecting subjects appropriately.

And then lastly, we recognize that a big part of moving studies forward appropriately and increasing our efficiency in this process is through improved communication with our sponsors. And you're going to hear about some of the ways in which we're trying to do that.

A great deal of it just has to do with, frankly, we're in the middle of an IDE review, we come up with an issue that we think could be resolved. Rather than going to the end of that review and sending a letter and requiring an additional cycle of review, there are times when it really makes a lot of sense for our review team to pick up the phone and speak with our sponsors and figure out if we can resolve this quickly through some interaction.

So that's an important shift for us to really focus on that. And I think that these three bullets, in combination, are a major part of why we've seen the improvement that we've seen that I'm about to show you.

And then in the area of early feasibility studies, we have also established expert coordinators within the Clinical Trials Program and then within each device division, and I'm going to talk about that later on today.

So I'm going to walk through a little bit of detail about what the FSOP is that we put in place and how that's working for us. So for example here, let's say that we have a 30-day IDE review that's in round one. So this is a new IDE that has come to FDA.

And let's say that for several reasons we disapprove that IDE. So once we disapprove that IDE, one of the things that we are now offering is within ten days of that decision, we are offering to have a teleconference between the review team and the sponsor to make sure that, that sponsor fully understands what we said in that letter.

This isn't to entertain new proposals. This isn't to go into depth about a new way to address some questions. This is to make sure that we are all on the same page, in terms of what FDA was concerned about when we sent that letter.

And I can tell you that I've sat in many of these meetings, and it is absolutely the case that these meetings, not always but in many cases, resolve a point of unclarity that was not uncovered prior to that meeting. And had we not had that meeting, I believe, would have had additional cycles required to resolve that letter.

And of note, if we disapprove in the first round, or if we approve a study with conditions in the first round, one of the changes that we have made to the SOP, really just a couple of months ago, is that the Clinical Trials Director can look at that decision after the fact and decide whether they have questions that should result in a discussion with a review team and, potentially, a modification to that decision.

So now let's say that we are in round two. The sponsor has come back and responded to that disapproval letter, let's say. And we have a decision that is either a disapproval or approval with conditions.

And I should clarify the meaning of approval with conditions for those of you who may not know. Approval with conditions means that the sponsor is allowed to start that study, so long as they agree to respond to certain conditions or questions that we have in our decision letter within 45 days.

In a disapproval decision, the sponsor is not allowed to begin that study until they respond to our letter and either receive an approval with conditions decision or a full approval.

One of things that we at FDA have really recognized, and we've heard loud and clear from many of our external stakeholders, is that approval with conditions, even though we recognize that sponsors are allowed to start those

studies, in many cases it turns out to not be so practical for them to actually do that.

Many other stakeholders have concerns about approving studies that have conditions outstanding. For example, IRBs in many cases don't support studies starting that are approved with conditions.

And many sponsors, frankly, feel concerned about starting a study that may need to be modified based on continued discussion about the approval with conditions deficiencies.

And so, I think approval with conditions is in many cases is a lot more like disapproval than it is like approval, in terms of the functional outcome. And so I think that that's an important recognition that FDA has made. And every time I've said this in a sponsor setting, I've heard loud and clear agreement there.

So, again, back to my round two example, let's say that we either disapprove that study or we approve it with conditions. So in this case, by definition according to our SOP, I'm going to review those letters.

The Clinical Trials Director is going to review those letters and likely meet internally with the team to ensure that we're in the same place, and also that we're doing everything we can to move that study forward.

A lot of those discussions are I concur with the letter, but what are the next steps? How are we going to move forward? Are we doing everything we can to prepare the sponsor to come back in that round three submission with something that we can appropriately approve?

And so once again, that sponsor is offered a telecon to make sure that they are fully aware of where we were coming from in our concerns, and that they are as prepared as they can be to respond.

So now let's say we're into round three. And so this is where we are trying to not have as many of files in that area. We are hoping to reach appropriate approval in round one as often as possible, and in round two where that isn't possible. In some cases, the right decision is still disapproval or approval with conditions.

So now we're in round three, and this is really more of an all-hands-on-deck sort of approach, where the Clinical Trials Director is now involved during the decision, during the review process, is engaged with the team prior to that decision being issued, and really making sure that if we're going to say no once more, we are all on board that this is the right time to do this; this is the right reason for saying no; that we are doing everything we can to move things forward.

And, again, for this stage and on forward, we will offer the sponsor telecons to resolve any points of - any questions that they may have about what was in our letter.

So what we're really hoping is that this program and elements of this SOP will help ensure consistency in our decision making, facilitate sharing of best practices across divisions, encourage higher levels of interaction, and to help prepare the sponsor to respond to our questions.

So prior to the existence of the Clinical Trials Program, there wasn't a formal way for divisions to learn from each other in the decision making that they

were rendering for IDEs. We think that this program will be helpful in that way, and we think that already it has shown some benefits in that regard.

So let me talk a little bit about we've seen in terms of our goals and our results for FY14. We specified goals for FY14 and FY15. First I'll talk about FY14, which of course recently passed. And these goals were compared to FY13 performance.

And we had two specific goals. We sought to reduce the number of IDEs requiring more than two cycles to an appropriate full approval decision by 25%. And I'm going to show you these results graphically in a moment, but we actually exceeded that goal by - with a 34% reduction.

Our second goal was to reduce the overall median time to appropriate full IDE approval by 25%. So that median time includes the time where the IDE is with the sponsor as well in between cycles, before they respond back to our letter.

And, again, we met that goal in quite dramatic fashion with a 53% reduction in the overall median time to appropriate full IDE approval. And, again, I'll emphasize that both of these goals are really focused on full IDE approval and not on conditional approval or approval with conditions. And that reflects our recognition that many studies really can't move forward until they reach full IDE approval.

So here's a graphical presentation. We have some historical data from FY11. I'm not showing FY12 because from the changes in the law from FDASIA really impacted the data from FY12. And I'm not going to go into the details there, but it's just not as clean of data.

So you can see that in FY11, we approved 14.8% of our studies within two cycles, fully approved. In FY13 we had dramatic improvement there, 43.5% fully approved within two cycles. A lot of that reflected changes in the law that happened in FY12.

And then you can see the change from FY13 to FY14, which I think is in large part reflective of the efforts that CDRH has undertaken in the past year. And you can see that we went from 43.5% fully approved in two cycles, to 62.7% approved within two cycles. And, you know, we're pretty excited about this performance. We think it really reflects a validation of the efforts that we've put in over the past year.

Here, I'm showing median days to full study IDE approval, and again, you look at where we were in FY11, our median time to fully IDE approval was 442 days. In FY13, that was dramatically improved to 215.

And then, again, from FY13 to FY14, another really dramatic improvement to 101 days median time to full IDE study approval. And so, again, this is pretty exciting information for us, recognizing there's still more to do, but I think we're on the right track.

So now talking about 2015 goals, and really emphasizing that these are very ambitious goals, seeking to continue that trajectory of dramatic improvement. Compared to FY13 performance, we're seeking to reduce the number of IDEs requiring more than two cycles to an appropriate full approval decision by 50% and reduce the overall median time to full IDE approval to 30 days.

So that's a really notable goal because, as I mentioned earlier, a cycle of IDE review is limited to 30 days. So essentially, what we're saying with this goal is that we are seeking to have at least 50% of our IDEs approved fully within

one cycle. That's a very ambitious goal, and I'm going to talk about some of the ideas we have for how we might seek to get there.

And then, lastly, we have established a performance goal for early feasibility, first in human studies. And that is really just to increase the number that we see submitted to the FDA. And I'm going to talk right now about why that's important and how we see that we might get there.

So the Early Feasibility Program is really focused on studies that are generally a small number of subjects, and they're studies for devices that are often early in development, typically before the device design has fully been finalized.

It doesn't necessarily involve the first clinical use of the device, but, really, the thinking here is that these are the small studies that are helping to lead to the final development of a device.

We may be in a situation where all of the animal and bench testing that could reasonably be done to move a technology forward has been done, and the next step isn't a larger study.

The next step is just studying this device in a few patients to figure out if there are small improvements that can be made to the device itself or how it's used, so that we can move forward with those larger validation studies.

So there are a lot of different insights that can be gained from these studies, and here are some of the kinds of ideas that we have for that: Human factors, operator technique, challenges, general safety of the device, potential for device failures, whether the device performs its intended purpose, therapeutic parameters for use of the device, and patient characteristics that may impact device performance.

So why focus on early feasibility studies? This really reflects our recognition that early feasibility is a very critical step in the device innovation and development process. And when device studies, such as these, are conducted in the US, these important technologies can really become available to U.S. patients sooner.

Frankly, we recognize that many of these studies, historically, have been done in other nationalities, other countries. In some part that's a reflection on the kinds of regulatory burden that is perceived in obtaining FDA approval for these IDEs in the U.S.

And so we are taking a really close look at that to see if there are ways where we can adequately protect subjects, but be more flexible to allow these studies to continue and to be initiated in the U.S.

So what are the kinds of things that we're doing to support that effort? We issued a guidance to outline our thinking on the early feasibility process and how we can be more flexible to allow those studies to be approved in the U.S. And I'm going to walk through some of the concepts from that guidance.

As I mentioned earlier, we have established and trained early feasibility study experts in each of the ODE review divisions, and our Office of Device Evaluation. So each device area has experts that have been trained in early feasibility study concepts that can assist both the sponsors and, frankly, also the review teams, because this thinking is really new for many folks within the agency, as well as those outside.

And we view this as an important training opportunity where we want to have experts in house in each of those divisions so that we can help develop that

training. And we are currently developing a CDRH learn module, which is our web available training tool focused on early feasibility studies.

So the key principal from the early feasibility study guidance is that approval of an early feasibility study IDE may be based on less nonclinical data than would be needed to support initiation of a larger clinical study of a more final device design.

So really, the thinking is that while we may be accustomed to asking for full validation in certain areas, particularly in the nonclinical data areas, there may be times where that is either impractical or really not the best place to be, given the stage of study that we're in. And I'm going to talk about that a little bit more in the next few slides.

And the guidance also outlines a regulatory tool kit that enables sponsors and regulators to think in new ways about device development. So we are inviting sponsors to justify that the appropriate evidence that they need to move forward is provided.

And we're really allowing for timely device and clinical protocol modification. We have some special variations to how we typically review IDEs, so that changes that should be made during the course of study can be implemented quickly and not stifle device innovation.

So really it boils down to the right testing at the right time. So we recognize that comprehensive testing during early phases of device development may add cost without significant return.

In many cases, the device design is not finalized, and asking for comprehensive testing in a certain area when the device design changes that

are going to occur based on this study may impact that testing, may mean that certain testing can and should be deferred until a later time.

So it may be acceptable to defer some of that testing until the device design has been finalized. And in many cases, we ask for early feasibility studies to incorporate additional risk mitigation strategies that protect patients, as compared to a later pivotal study in order to account for some degree of increased uncertainty in certain areas.

So what does this process look like? This is really, again, sort of an all-hands-on-deck kind of process, where we recognize these studies are very, very important to move forward, and we are making it a very high priority to be there to help sponsors move through this process.

And really, I'll start by saying that this is really recognition that many of the most innovative devices are being developed by sponsors who have some of the least amount of experience with FDA.

And that's a really important thing to keep in mind for our teams, because many of these folks have never interacted with FDA before. They're developing very innovative devices. They're very excited about their technology, but they may not fully understand the regulatory hurdles that they will encounter in moving forward with the IDE process.

And our job here is to really help them, to hold their hand a little bit, to explain the process and to really be as flexible as we can to move those technologies forward, while still protecting patients.

So we ask that the sponsors contact the early feasibility study coordinators and interact informally before we even start the formal process. That conversation

generally consists of discussing the early feasibility guidance and the policies, the principals that it's founded upon, any help that the sponsor may need, in terms of understanding what we're calling the device evaluation strategy concept and developing a device evaluation strategy table.

So what that is, is really a document that we're asking early feasibility study sponsors to provide the FDA that really tells their story about how they view the device and the testing, the risks that might be incurred, and how those risks are mitigated, that really walks through why the sponsor thinks that they have conducted the right testing at the right time, why they think that their plan is the right plan.

And so we want to help them develop that table and that document so that we can really hit the ground running when that submission comes in the door. So we're trying to prepare them, as best as possible, for the more formal interactions that will come in the future.

The next step after we've had that informal interaction is for them to submit a pre-submission, often called a pre-sub and that, really, is to, you know, it's one step forward in formalization, but we're not at the formal IDE yet.

So the idea here is to reach agreement on the information that's needed in the IDE submission. And sometimes this pre-sub has multiple supplements as different elements of the IDE submission are discussed.

Really we want to make sure that when that IDE hits the ground, when it arrives on our doorstep, that we've had the necessary discussions so that no one is surprised. We're able to hit the ground running on our review of the IDE, and hopefully come to a decision that appropriately allows that study to move forward very quickly.

I should also mention that while we're trying to be interactive with all our IDEs and really trying to encourage that culture globally, there is particular effort in the early feasibility study arena where again the focus is really on making sure that if a question comes up, we're picking up the phone. We're interacting with the sponsor. We're making sure that everything we can possibly do to move that technology forward is being done.

So here I have a list of the experts that we have in each of our device divisions. You'll see at the top we have Dr. (Andy Farb) and Dorothy Abel. They are leaders for the early feasibility team. They were the primary authors in the early feasibility study guidance and they're both in the room with me today.

So if you have any questions in that area, I will surely be passing the mic in their direction. You see that for each of the device divisions in ODE we have multiple experts, and then we also have experts in our Office of Finance and Engineering Laboratories, because really a lot of our questions have to do with the nonclinical testing and in many cases that involves reviewers from that office.

And so we have some experts there, as well, to help with those consulting reviewers who play an integral part in the review of those IDE submissions. I should mention that this is the list as of today, but this is a fluid list.

We - and actually I view that as very much a good thing that we will continually evolve and at some point this list will change to be different experts. And we will be training up different folks in our review divisions to become experts in this area and I think that's a really wonderful thing.

So if you have a device and want to be at divisions and you contact one of these folks and it turns out that that person isn't doing that anymore, than I strongly encourage you to either contact me or (Andy Farb) or (Dorothy Abel) to figure out who the right person is that you should be speaking with.

So where are we going to go in the future? So I think one of the key points is that we're going to continue doing what we're doing for one. So we're going to continue to monitor the performance in our IDE decisions.

We're going to continue to use the SOP that I walked through to take a very close look at the decisions we're making and make sure that we're in the right place, that we're being as flexible as possible and that we are interacting in the optimal way with our outside stakeholders.

We're also going to have a continued effort on the early feasibility study IDEs, as I just discussed. Another effort that we are currently undergoing is developing a draft benefit-risk guidance for IDEs.

In a few slides I'm going to show you a list of some important guidance documents that are already out and final. One of those is the IDE decisions guidance which really is a walkthrough of the kinds of decisions we make and how we make them, and really a relatively technical document, nuts and bolts of what happens in the IDE review process and what an external stakeholder, a sponsor, might see in an IDE letter and how to understand that decision.

In contrast, the benefit risk guidance document that we're drafting right now is really more of a philosophical document that explains the thinking of how we reach an approval or disapproval decision.

What are the kinds of factors that play a role in reaching that decision? And how we roll in the concept of uncertainty into that decision, and how greater uncertainty might be acceptable if there's the potential for greater benefit, and those sorts of concepts.

So look forward to seeing that draft guidance coming out in the hopefully relatively near future. I think it'll be an important document and we look forward to comments from folks like you all on what your thoughts are on this philosophy and how we describe it in this document.

We also recognize that we want to continue the development of additional, clinical trials training both internal and external. So for our review staff, as well as for our external stakeholders.

As I noted at the beginning and as you've see at the bottom of most of my slides, with regard to the external stakeholder training, we really want to hear from you and help us shape that. You know, webinars such as these are part of that training.

Our CDRH learn module that we're developing for early feasibility studies is part of that training, but we really want to hear from you in terms of what you think you, as external stakeholders, can best utilize in terms of information that comes from us.

With regard to internal training, there's a lot that we have historically done that we do very well. There are some areas that we have done less well, historically, that we're really trying to focus on now.

I'll just highlight one in particular right now, which is really developing some training on the clinical trial ecosystem for our review staff. So as you may know, many of our review staff, most of our review staff, are engineers.

They know a lot about how to review the technical aspects of an IDE submission. Many of our review staff are clinicians, they know a lot about how to review the protocol. But many of our review staff, frankly, most of our review staff do not have a lot of experience with the actual roll out and implementation of a clinical trial out in the world.

And we feel that, while we can't give them that experience, we do feel that we need to improve our training in that area so that the impact of our questions, the complications and challenges that are encountered out in the world with an IDE is turned into a functioning clinical study better understood and rolled into our reviews.

And so that's something that we're really looking in improving in this next year, and we're pretty excited about bringing that as training to our staff. And then, lastly, another area that we view as really important is submission quality improvement. And I'm just going to spend a couple of slides right now talking about what we mean by that.

So I think I pointed out and you may have noticed that our FY15 goals in terms of IDE approval rates are very ambitions and are really going to require work not just from FDA, but also from IDE sponsors.

The improvement that we saw in FY14 I think reflected a lot of the lower lying fruit that FDA could make in terms of improvements to its process to reach more expeditious approval decisions.

But we have a submission quality challenge that I think will need to be addressed in order to see some of the dramatic improvement that we're hoping for FY15. So this reflects a couple of different concepts here. One is that many IDE submissions I'll call it fail to tell the sponsor's story.

And what I mean by that is many IDE submissions include a lot of test reports and a lot of data for FDA to review, but not a lot of narrative explaining how the sponsor views these data, and why the sponsor thinks that these data are the right data to move the submission forward.

And you know what I've often phrased it as in many cases we get an IDE submission where the sponsor is saying, "FDA, here's what I have. Is it enough?" And really, what we want to do is get to a point where the sponsor comes in and instead says, "FDA, here's what I have and here's why I think it's enough."

And so that contrast is really important. In many cases, we have several rounds of review where we ask a question because we identified an issue, say, in the animal study and the sponsor responds by saying, "That's true, FDA, but we did this other test that showed that this was an anomaly, or that this was mitigated by this other thing we're trying to do."

And that may be an appropriate response. It would be even better if it were told in the initial submission, such that we could all get to that point of agreement much more quickly. Next is that many other submissions really fail to provide basic information needed to support FDA's IDE review. And this is really a problem that we need our external stakeholders to partner with us to improve.

We recognize that interaction is important and it can address many minor issues and reach resolution during IDE review, but improvements in submission quality are really a critical component as well, because in many cases the IDE submission is so lacking that we really can't move forward without issuing a disapproval letter and the sponsor responding with a submission that actually provides that basic information.

So here are just some high level reasons that we have seen for IDE deficiencies. We are currently undergoing a more thorough look at some deficiencies that we've issued over the past couple of years.

I don't have specific data to show you right now, but I will point out that these are some of the high level, big, heavy hitters. So you'll see device description, mechanical testing, bio compatibility testing, and animal testing.

And I'll just highlight device description as one that is particularly susceptible to issues of submission quality. So here we're really asking, in many cases, not, you know, could you do something different or we disagree with what you did, or here's why this is insufficient.

In many cases, these deficiencies are instead, we don't understand what your device does. We don't understand its dimensions. We don't understand its materials. We don't understand the testing you conducted in a certain area.

And so we're not at a point of even conducting the review to determine whether we agree with what you've done or what your device does. We're asking a question that's just clarifying, because we don't understand the fundamentals to even really start that substantive scientific review.

And that's really a problem that needs to be addressed in order for us to move things forward in the area of approval of these IDEs. So here are some of the kind of questions that relate to submission quality that a highly quality submission should largely avoid in many cases.

So describe the device components and the materials. Describe the principal of operation and the key characteristics. Clarify the version of the device tested compared to the version for the clinical study.

This is a very common problem that we see where a device is modified during the course of testing. Perfectly appropriate, but it's very difficult for our IDE review team to figure out what version of a device underwent what test and whether the version difference makes a difference in interpreting those data.

Clarifying what testing was even done with a rationale for why it was the right testing and providing adequate description of that testing, in terms of the test conditions, success criteria, and results.

So you see that all of these bullets aren't about questions where FDA is saying, "We disagree." It's saying, "We don't understand enough to know whether we disagree." And these are the kinds of questions we would like to circumvent in the future as best possible.

And we are currently trying to figure out the best way to do that and that's going to be a big focus of our next year is to figure out how we can do that in a practical way, and work with our sponsors to come in the door with better submissions.

So in conclusion strengthening the clinical trial enterprise is a very high priority for CDRH. It's one of our three strategic priorities for FY14 and '15.

We've made major progress in the past year. However, we recognize that a lot of work remains and future progress is very ambitious and it's going to be a joint effort between FDA and our external stakeholders.

So as I mentioned, here are several really important guidance documents that can be very helpful to sponsors and other external stakeholders as they're trying to understand our processes and our priorities.

So the first is the decisions guidance document for IDEs. This really walks through the kinds of decisions we issue, what they mean, and how you may see them conveyed in our letters. So I strongly recommend this both for sponsors and IRBs and anyone else who is involved in the IDE decision process and needs to interpret FDA's letters.

The next is the guidance that I referenced regarding early feasibility studies. So it really walks through both the concepts in terms of how we think about early feasibility studies and also some of the practical tools that we've implemented to make the process work.

The next one is design considerations for pivotal clinical studies. So that really talks about how we think about designing studies that can support future marketing applications. And then the last one is an evaluation of sex-specific data in medical device clinical studies.

So we're about ready to turn to questions and rather than sitting on this question slide, before I switch I will point you to this email address so that if you don't get your questions answered today, please email this email address and we will send your question to the right folks who can address it.

But then I'm going to stay on this last slide while we go through the questions. And again it's just a reminder that we really need your help to figure out how we can best educate our external stakeholders and reach out with regard to education and training and communication about what we are doing in this arena and what you should best know to play a role.

So again this is a very short survey. I'm going to leave the link up and I really encourage you to take a few minutes to give us your feedback. We have a team of folks who are very interested in receiving that feedback. And with that I will close and we will look forward to hearing your questions.

Coordinator: All right. Thank you. At this time we are ready to begin the question and answer session. If you would like to ask a question, please press star 1. Please record your name. To withdraw your question, press star 2. Once again star 1 to ask a question. One moment. And our first question comes from (Nicole Baker). (Ms. Baker), go ahead. Your line is open.

(Nicole Baker): Sorry. I had a technical question early on but we resolved it. So I withdraw my question.

Coordinator: All right. Thank you. Next question is from (Mark McCardy).

(Mark McCardy): Hi. Thank you very much for taking my question. Owen, a question about IRBs and the reluctance to engage in IDE studies that have the approval with conditions label on it. To the lay person there might be two things involved there. One might be that, you know, this situation means extra work for the IRB.

I think another possible reason for reluctance might be just that an IRB is reluctant to engage a study that doesn't have a full FDA seal of approval, so to

speak. Can you talk a little bit about the IRB reaction to an approval with conditions IDE study?

Owen Faris: Sure. I'm happy to. I've actually had extensive conversation with the IRB community. I've given a talk at the PRIM&R meeting which is the large IRB meeting for the past three years about this very issue.

And I think there are a few reasons for why IRBs are sometimes hesitant to grant approval for studies that FDA has granted approval with conditions. One is frankly that those letters are often very complicated. And so we often issue several deficiencies in there that on the surface can look like deficiencies that are very concerning, in terms of protecting subjects.

We've reached those decisions and said that the study is approved with conditions based on a very detailed review. And we've come to the position, if we've issued an approval with conditions, that it is appropriate to move that study forward.

But that said, those deficiencies sometimes are very difficult to interpret in the vacuum of not having the review in front of you. And so an IRB sees that letter. They see some questions in there that the sponsor still has to address.

They deal with subject safety and it's sometimes difficult for the IRB to come to the same conclusion without all of the information in front of them. And frankly sometimes all of the expertise in the room that, that deficiency doesn't rise to the level of needing to be resolved prior to enrolling subjects.

So I think that that's probably the biggest issue. I think, frankly, to a certain extent there's a little bit of an education piece as well of not really entirely

sometimes understanding what FDA means with an approval with conditions letter.

I think that that's really shifting. Historically our approval with conditions letters weren't worded optimally in terms of explaining what we meant by that decision. I think that's improved dramatically over the past year or so. And so I think that issue is becoming less and less.

There certainly are some IRBs that are very comfortable with that model. But I have heard loud and clear from many IRBs that they really want to know that FDA has no safety concerns prior to that study moving forward, rather than just only minor ones that FDA has decided are sufficient to resolve while the study is getting started.

(Mark McCardy): Okay. Great. Thank you very much.

Owen Faris: You're welcome.

Coordinator: All right. The next question is from (Danny).

(Danny): Thank you very much for taking my question. I have actually a couple questions. As you focus more on the clinical trials aspect of the devices, is FDA considering hiring more personnel or reviewers in order to try to shorten your review times?

And secondly you said that for the early feasibility studies you'll be developing a module. Could you talk a little bit about that module in terms of what will be in that module and when you plan on getting that out to, you know, people who might be able to use that?

Owen Faris: Sure. So I'll take the first part of your question, and then I will send the second part over to our early feasibility study experts. So your first question deals with hiring, recognizing I think that you rightly recognize that much of what we're talking about here is very labor intensive and really requires a lot of time and effort on the part of reviewers.

And we absolutely recognize that and frankly this isn't a problem that is isolated to IDEs. We're also trying to improve upon our performance in many areas of device review and that requires more staff.

So we are doing a lot of hiring and that has been extremely successful. We have a lot of really wonderful new reviewers that have come on board in the past year or two and that effort continues very successfully. So I'm really excited to bring a lot of those folks on throughout our review divisions.

And we are also expanding within the clinical trials program so that we have the support to be able to provide to our review staff as they make their - as they conduct their reviews. So yes hiring is a perpetual issue. We're doing a lot of it, recognizing that to do what we need to do we need to have the staff to do it. And now I'm going to turn over to (Dr. Farb).

(Dr. Farb): Thank you, Owen. The CDRH learn module, which is in process and we're hopeful to be out and available in the first quarter of 2015, will cover the early feasibility study guidance and in detail as a teaching forum that will help sponsors and investigators navigate the process.

There'll be six submodules within the entire CDRH learn program, starting with the introduction to the program and why the early feasibility study guidance was developed, discussion about the process of really getting into

details about how the program works with respect to interactions of sponsors with the early feasibility study representatives, as well as the review teams.

Two detailed modules on the report of prior investigations into the device evaluation strategy. The next module will be about the clinical protocol, including specific patient protection measures.

And then finally a module on how the early feasibility study guidance has new policies to facilitate changes to the device and procedure during the conduct of early feasibility study guidance - early feasibility study, study itself.

(Danny): Thank you.

Coordinator: All right. Next question. Sri Koushik. Go ahead, sir.

Sri Koushik: Hi. This is Sri Koushik. Thank you for your presentation. I really enjoyed it. I just have three questions actually. One starts off with the early feasibility study, specifically with regards to the DES that you guys were talking about. That's sort of - I mean all the data that goes into it sounds like you need a risk analysis more than actual submission of real data. Am I correct in gathering that information - is that a correct assessment of it?

Dorothy Abel: Yes. It is more of a risk analysis that you go through in order to determine the testing necessary to support and justify study initiation.

Sri Koushik: So then the question is that, you know, follow-up question to that is basically so that if you are looking at a device that goes into human beings and it's very specific to a human being, the chances of you actually getting any animal data is probably, you know, maybe not worth going into to try to assess safety.

Are you guys going to sort of, on the early feasibility study, like first in man studies can we sort of try out our device? Because it really doesn't make sense trying to develop a device that will go into an animal, then change it to go into a human being. See what I'm saying?

Dorothy Abel: So what we ask - excuse me. I'm sorry. What we ask you to do with device evaluation strategy is to breakdown what the device needs to be able to do and the information that you have to show that it should do that without having any problems.

Traditionally, part of that assessment has been animal studies, but we recognize with really innovative products there may not be an animal study that actually can predict clinical outcome.

But you may be able to get some information out of an animal model to address specific attributes and potential failure modes. So you would need to work with the review team to try to figure out what information would be appropriate given your particular product.

Sri Koushik: Okay. The second question has to do with the checklist that Owen spoke about in the end of the, you know, the presentation. Do you guys ever - I mean, I'm sorry, you guys give a list of things that you normally see going wrong when IDEs are submitted.

What I wanted to know is if you're going to release something like a checklist or something that, you know, sponsors can go through saying, okay, have I checked - have I done this correctly, have I done this correctly down the line. That way it would be easier to know that, you know, to avoid the common pitfalls. It's more like...

Owen Faris: All right. So you're pointing to an area of very active discussion right now within the agency. These are the exact kinds of questions that we are engaging in right now. I don't have an answer to your question.

We recognize there's a quality issue with many submissions. We recognize that it won't be fixed without us communicating to our external stakeholders in terms of better understanding what we see as the fundamental issues. We have to figure out the best way to do that and stay tuned.

Sri Koushik: The last question is, of course, the benefit-risk guidance. Do you have a timeline on when you think it might be out? First quarter? Second quarter?

Owen Faris: Predicting when a guidance leaves the agency is a very dangerous thing.

Sri Koushik: Okay.

Owen Faris: So I can say that I hope soon and I'm sorry that I can't give you anything more than that.

Sri Koushik: Thank you very, very much.

Coordinator: All right. Next question is from (Elizabeth Sheehan).

(Elizabeth Sheehan): Hi. Could you clarify the role of the teleconference in the round of the IDE submissions? If I was understanding that correctly, the teleconference is used to perhaps clarify questions that came in the letter from FDA but it doesn't replace that the sponsor has to again submit for another 30 day round of review. Is that correct?

Owen Faris: That is absolutely correct. So their major point with that telecon is that it is to clarify to the sponsor anything that - any points of ambiguity or uncertainty with what we conveyed in that letter.

And they're thinking of why it happened so quickly is because that's exactly what it is. It's not to review new data. It's not to review a response. We can do it a couple of days after the letter went out, because it's fresh in everyone's mind. And really all we're doing is making sure that everyone is on the same page about what was intended in that letter.

Frankly, you know, sometimes that discussion goes a little bit further to talk about how the sponsor might be thinking about a response, but the main focus is to make sure that we all understand and are on the same page about what was intended. So that the sponsor can be prepared to formally respond.

(Elizabeth Sheehan): Right. Thank you very much.

Coordinator: The next question is from (Kristen Hilton).

(Kristen Hilton): Hi. I was wondering if you could comment on the process of amending the study once it's approved. You gain the IDE approval which then helps with IRB approval. What's the process if that study and the use of the device perhaps might change?

Owen Faris: Right. So we see that very, very commonly where we've approved a study and then for some reason something needs to change, either to the protocol or how the device is being handled or used or frankly sometimes to the device itself during the course of the study.

There is a supplement to the IDE that the sponsor submits and just like the original IDE FDA has 30 days to review it. And just like the original IDE, we can approve it, we can approve it with conditions, or we can disapprove your proposed changes.

And in either case you would get a letter. If we are not fully approving it, that letter would have deficiencies that you would answer. And hopefully we would eventually get to the point where you would get full approval for whatever changes you propose. So it works a lot like the original IDE review. And that's described in a lot of detail in the IDE decisions guidance that I referenced.

(Kristen Hilton): Okay. Thank you.

Coordinator: Next question is from (Sharon Warren), I believe.

(Sharon Warren): Yes. Am I on the line now?

Coordinator: Yes.

(Sharon Warren): Hi. Thank you so much for this presentation and thank you for everyone else's questions. I think they've been - my head has been in much the same space. I just wanted to - it was a comment that I wanted to make and perhaps have you - or an observation that I wanted to make and perhaps have you speak a little bit more about it.

It sounds like that you're actively making steps within the FDA to encourage more interaction with sponsors for clinical trials. What - does this extend to - perhaps the question in here is does this extend like right through the design process for like animal studies, if that's a factor; the human factors, any

studies that are done for human factors, engineering or feasibility; right through the 510(k) submissions and for PMA submissions?

Does it extend across that whole line? Is that a general approach that the FDA is actively trying to change?

Owen Faris: That's a great question. So, you know, if you think back to the three strategic priorities that I described in one of my first couple of slides, one of them was focusing on clinical trials. One was focusing on striking the right balance in pre- and post-market decisions so, you know, marketing decisions, marketing application decisions.

And then another was on customer service and making sure that we are interacting optimally both with our internal and external stakeholders. And I think this all reflects the consistent philosophy that we do want to be more interactive throughout the process. You know, we've identified specific goals and targets for the IDE process in particular, but it does extend throughout.

And so a lot of the things you talked about in terms of nonclinical testing and human factors and all those sorts of things are perfect topics to have as part of the pre-submission discussion and can, in fact, you know, play a major role in a successful IDE submission that follows after that.

And so we really do want to be far more interactive than we might have been several years ago and just, you know, continuing to improve in that direction. We have a very interactive culture here that we want to continue to foster and develop. And I think that, that does extend through the marketing process as well.

So whether it's a 510(k) submission or a PMA submission, we don't have specific targets in that area right now, but the philosophy is consistent that we want to be offering service to our external stakeholders to help them reach appropriate approval. And that extends through getting these devices out onto the market.

And obviously if we improve upon the clinical trial enterprise but we still don't move these innovative technologies onto the marketplace, then we haven't really done a lot to help patients in the U.S. And so we definitely recognize that this is one part of a much more holistic approach.

(Sharon Warren): Thank you.

Coordinator: All right. Next question is from (Tepel).

(Tepel): Hi. Thank you. I have a question regarding a non-significant risk feasibility study to be used in a submission. So it seems to be good practice to utilize design control for the design of the device, but it's not clear in any of the guidance or the regs if that's an expectation or a requirement with FDA. I was hoping that you could comment on that.

Owen Faris: I'm not sure I fully understand your question. We could try to clarify it here or maybe it might be better for you to write your specific question to the email address listed and then we'll try to have an offline discussion in more detail.

(Tepel): Okay.

Coordinator: Our next question is from (Barbara Cox).

(Barbara Cox): Hi. Thank you. You mentioned about the early feasibility study coordinators that, again, they're kind of specifically trained to handle questions from a sponsor. I wonder if this is going to be part of their regular activity that is different from, say, what reviewers have in terms of their 30 day letters and (180) day letters.

Is that informal communication kind of a milestone for them to deliver to the sponsors, just like them having to meet their deadlines for 30 day letters and other types of kind of regulated timelines?

Owen Faris: So thank you. It's a good question. I'll start and then see if (Andy) and Dorothy think that I haven't fully answered it. So, you know, we have designated this role for these expert coordinators within each of the device divisions as part of their workload.

And if there's a recognition that this will take a significant portion of their time, they're still doing review work and leading review efforts, but this is an important part of what we're trying to accomplish as a center.

And we recognize that we need to prioritize that by allowing these reviewers to take the time both to develop their expertise and then frankly to use it. And so this is part of their work when they're spending time interacting with sponsors, when they're spending time interacting with review teams and training in this area.

This is - their workload reflects that this is an important, high-priority and is done as, you know, part of what we're prioritizing for how they spend their time.

(Barbara Cox): Thank you.

Coordinator: All right. Next question is from (Dane).

(Dane): Yes. Hi. Thank you very much. This question may be a little wide of today's excellent presentation, but it is related. There are academic medical centers that study approved devices for safety and efficacy, and whether or not the IDE regulation even applies can turn a lot on if that investigation is conducted within the current labeling.

That labeling is not completely easy to determine in all cases. And I'm wondering - that's really my question. What is the best way to determine the - if an investigation is being conducted exactly per the approved the labeling and when the IDE would be necessary?

Owen Faris: I'm going to turn that question to Dr. Soma Kalb, who is the Director of our IDE program.

Dr. Kalb: Thank you for your question. The question about whether a study or a device is being used in accordance with the labeling is often a gray area and it's subject to interpretation. Initially the sponsor makes a significant risk or non-significant risk or exempt determination based on their interpretation of the way the device is being used.

And then the next step if a sponsor believes that a study is exempt, is for the IRB to review that as well. If the IRB doesn't agree with the sponsors' determination, then the question can be sent to the FDA and FDA can make a study risk determination.

It is - there are many factors that come into consideration when you're looking at whether something is being used in accordance with the labeling.

Sometimes a particular use - the labeling might be silent on a particular proposed use and the risk that might be imposed by that different use might be considered.

So it really needs to be considered on a case-by-case basis, and I would point you to one guidance that is available that may help with that sometimes is called - it's referred to as general to specific. You can perhaps Google that and see if you can find that guidance or you can send an email to the DICE link that was provided earlier.

(Dane): Okay.

Dr. Kalb: There's also a helpful guidance on SR and NSR determinations and frequently asked questions about medical devices that speaks a little bit to exempt studies that might be helpful.

(Dane): Sure. Thank you for that guidance. It's just you don't even reach the question of the SR and NSR determination if you are exempt. But I do appreciate the other - in the case of ambiguity does FDA prefer to have the question put to them to resolve it in all cases, or should the institution just make its best educated guess?

Dr. Kalb: I think that's at institution discretion. FDA is available to help and I think that, you know, we do frequently see those types of requests. Sometimes the institution may go ahead and submit an IDE, and you will also get that determination in our response letter if we believe it's exempt.

(Dane): Very good. Thank you very much.

(Barbara Cox): All right. Next question is from (Richard). Okay. We'll go on to the next question. (Laura)?

(Laura): Hi. Thank you. Can you just comment as to the level of detail that is required with regard to the manufacturing data? For example, would the final sterilization validation be included in the IDE packet for FDA to be able to approve use of a sterile device and have that documented that it's sterile, or could you just include the sterilization protocol and the standard that you're complying with?

Dorothy Abel: Can you please repeat your question?

(Laura): Sure. I'm not sure if you can hear me well. Can you just comment as to the level of detail regarding the manufacturing data that needs to be included in the IDE application? For example, must final sterilization validation of your device be included?

Owen Faris: I think that really is very device and study specific in terms of the degree of validation that would be needed based on what the risks might be for that device and that study. So there are certainly times where we say that we want to see full validation, because we have a lot of concern.

But there are other times where some lesser amount of validation might be appropriate considering the risks of the device and what the potential therapeutic options are. It gets back very much to a risk and benefit assessment.

(Laura): Okay. Thank you.

Coordinator: Next question is from (Deborah).

(Deborah): Hello. This is (Deborah). I'm calling about a question that I have regarding an approval with conditions. The letter conditions are pretty minimal and (unintelligible). However, there was a very expensive list of additional recommendations after or following the letter, some of which were not terribly clear.

And just wondering what the best way to, per the new guidance, the best way to approach that?

Owen Faris: Yes. That's a great question. And I think you will see some guidance regarding the meaning of those questions if you look at our IDE decisions guidance. But this really reflects some changes in the law that I briefly referenced in my talk today that occurred in the middle of 2012 that changed some of the criteria by which FDA could disapprove a study.

And essentially FDA no longer disapproves or approves with conditions a study for reasons that are associated with the study may or may not be willing - may or may not be able to support a future marketing application.

So let's say that we think that the device has been adequately tested in terms of safety and potential for effectiveness. We think that the study protocol adequately protects subjects. We think that this device is ready to be studied from a subject protection perspective.

But we think that there are issues with the study design that should be improved upon in order for the study to support it goals: For example, a future marketing application.

In that case those issues will not be deficiencies in the letter and will not impact our decision about whether to approve or not approve that study. But if we think those issues are important enough that we really want to recommend that the sponsor incorporate them, we'll put them as what we call study design considerations as an attachment to that letter. And we'll communicate that to the sponsor.

So if you want to address those so that we're all on the same page that not only are you doing a study that's sufficient in terms of protecting subjects, but you're doing the right study to achieve your goals.

And we're sort of all on the same page about that so that at the end of the day we can all look at the results and interpret them in the same way, then we strongly encourage you to respond to those study design considerations.

If you have deficiencies in your approval with conditions letter, you can respond to everything all at the same time and that's completely fine. You can respond to the conditions, the deficiencies, as well as the study design considerations.

If you have a full approval, but we still have some study design considerations, some recommendations, then you would submit - if you chose to respond to that, you would submit a supplement to that IDE that proposes changes to your study to address those concerns. And we would review that just like we would any other IDE submission within 30 days.

And at the end of that, tell you whether: One, do we approve those changes? And two, do we agree that you've addressed the concerns such that we now think you're doing again not just a study that adequately protects subjects but the right study to achieve your goals.

(Deborah): Okay. But with those additional recommendations and considerations, some of them I guess we're unclear to their meaning. But would you recommend would be the best approach to interact with the FDA and get some of that clarity?

Owen Faris: Sure. So they can be clarified during that ten-day call if, you know, you have a ten-day call offer by FDA to have that clarification meeting, we can certainly clarify those study design considerations.

If for whatever reason, you know, we're later out here and you haven't had that call or those questions didn't come up, you can reach out to the review team. And, you know, if they're minor clarifications the lead reviewer might say, "Well, you know, I'll get my clinician on the phone and, you know, we'll clarify this. You know, we'll have a chat, you know, in the next couple of days or something."

If they're more complicated and you actually want to talk about how you might respond and there's going to be a need for the team to review a proposal before they can give you feedback, then that's probably best submitted as what we call a submission issues queue submission.

So what - basically it's an informal submission that provides the information such that we can have an informed discussion. So that really depends on the level of your question, but if it's just a little bit of a clarification I would just suggest that you first start by reaching out to the lead reviewer and getting their best advice.

(Deborah): Okay. I appreciate that. Thanks.

Coordinator: Question from (Jerry).

(Jerry Prudhome): Hi. This is (Jerry Prudhome). Thank you for permitting me to ask this question. The early feasibility guidance authored by Dr. Farb and Dorothy Abel is really quite an elegant guidance and describes in detail the process.

It seems to be to encourage United States companies to conduct early feasibility studies in the U.S. rather than going abroad to conduct such studies, as had often historically been the case.

Nevertheless, the guidance does seem to require considerable data and information to be submitted in order for companies to obtain approval for such early feasibility studies. I was wondering if you could share with us some of the FDA experience since the issuance of this guidance.

For example, what proportion of IDEs in the last year have been early feasibility study IDEs? Are there any types of devices or review divisions that see early feasibility studies more frequently than others or if you could just provide us with any kind of other status update on the success of the implementation of this program?

Owen Faris: (Jerry), you've asked a really timely question. Right now we are very much right in the midst of gathering that data. I can't give it to you yet, but we're working on gathering it right now.

As you know that one of our goals is to bring more early feasibility studies into each review division, we've set a deadline of that of June of this year. And so we have to start figuring out whether we're on track to be doing that.

And the first part of that was to figure out exactly how we were going to define early feasibility studies in an objective way. We've done that and now we are going through our IDEs to audit which ones fall into that category and which ones don't.

It's a pretty Herculean task, but I'm pretty excited to see what the results will turn out to be. I don't have it for you yet but please stay tuned. We recognize that that's something that not just you and others outside the agency want to know but we really need to know inside as well. Dorothy, do you want to say some more?

Dorothy Abel: Yes. I just wanted to add with regard to the amount of data that's necessary to support study initiation, we have certainly seen many projects go forward where the sponsors have been able to justify providing less data than we would see for a larger study like a pivotal study.

So using that device evaluation strategy we look at not just the testing on the final device design, but all other information that's available such as how the device was designed in the first place; any information that could be leveraged from a nonclinical standpoint, maybe from testing of prototypes; and also clinical information that could be available to the sponsors.

So we are looking at these projects differently and we have been able to do so successfully. Again we don’t have the metrics at this point in time, so we can tell you qualitatively that it does seem to be working.

(Jerry Prudhome): Thanks for that feedback. I appreciate it, Dorothy.

Coordinator: All right. Next question. (Flori Sida). Go ahead, ma'am.

(Flori Sida): Thank you. Thank you very much for the presentation. My question goes in relation to the established clinical trials program and the intention and the process being discussed. How can this apply to devises that are part of a combination product?

Owen Faris: So it sounds like to me you're asking really how does this apply when a device isn't strictly just a device, but is a combination product, presumably a combination product that resides primarily in CDRH?

So we treat those IDE submissions just like any other. So if it's in a combination product that resides in CDRH it fits under our metrics. It fits under all of these efforts that I walked through. It falls under my review post decision.

The only thing I would say about combination product reviews is they tend to be some of our more complicated. And because of that it is sometimes more difficult for us to be interactive during the course of the review.

And so those - that does sometimes present a challenge when we, you know, uncover issues. It sometimes is a little bit more difficult to try to resolve them during the course of the review. We still try. We still encourage our teams to do it.

But that, you know, when I'm looking at a decision that isn't an approval decision at the end of the day and I wonder whether the team went interactive and whether they tried to resolve things, frankly one of the factors I consider is was it a combination product. Because sometimes that presents an additional obstacle to having that be practical. Sometimes we're still able to do it.

(Flori Sida): And if the combination product is not to be reviewed by CDRH but by CDER would the same answer apply?

Owen Faris: So if it's primarily a CDER combination product where we are in an assist role, CDRH is in an assist role providing the device input, that would not be part of what we're talking about here.

(Flori Sida): Okay. Thank you.

Coordinator: Question from (Julia).

(Julie): Actually - yes, thank you. So the previous question actually provided the perfect segue to my question. My question is also related to combination products and the final approval will be through the CDER.

So my question is so if we're doing early feasibility studies for the device, which will be part of the device-drug combination product, do we need to submit IDEs or actually we need to do INDs?

Owen Faris: We're having some - we're turning our microphone on. Just one moment.

Dr. Kalb: Hello. Most often either an IND or an IDE is required. It's very rare that there would be both. And in order to determine which center has the lead for your product and whether it would be an IND or an IDE, you might want to submit a Request for Designation, an RFD, to the Office of Combination Products to determine the jurisdiction for your device or your product.

(Julie): And that's the case for even for a study that's done for device development, not necessarily having anything to do with drug yet?

Dr. Kalb: I'm not clear on what you mean.

(Julie): So basically if the study is to be done to determine the device development requirements, which is an early stage of the development of the product and the drug piece will come in later on. So basically the study is purely on the device. However, this device will never be put on the market without the drug.

So I guess my question here is for those type of early feasibility studies, do we submit IDEs or INDs? I guess you're saying that we may have to submit a determination of jurisdiction request?

Dr. Kalb: I think this is a pretty complicated scenario that you're describing. I'd suggest sending that question to the email address that was provided earlier and we can try to get an answer to your question through the Office of Combination Products.

(Julie): Okay. Thank you.

Coordinator: Okay. Next question is from (Neda).

(Neda Moody): Hello.

Owen Faris: Hello.

(Neda Moody): Hi. I'm (Neda Moody). And (unintelligible). My question is that if new thinking and strategy of clinical trials program at CDRH does it supersede device type specific documents released early by FDA or CDRH?

Like let's say (1919s) where three different phases of clinical studies are laid out and which are not aligned with this new thinking. So is CDRH going to

update those guidance documents which were released earlier to align with this new thinking?

Owen Faris: So our efforts certainly do not supersede and in my view aren't in conflict with our previous communications and previous guidances. Certainly early feasibility is an area that wasn't previously defined. We view it as a subset of feasibility studies, so sort of consistent with what we've laid out previously.

I'm not aware of specific inconsistencies. I'd be very happy for you to email any that you're aware of to us at that email address and we're happy to look at them. Certainly we want to resolve any inconsistencies. But I'm not aware of any inconsistencies or any ways in which the efforts that I talked about today run into conflict with anything that is currently our practice or has been conveyed.

(Neda Moody): Okay. Thank you. And I do have one other question. This might be too specific to a device but I'm going to ask it anyways. And that's regarding clinical investigation requirements of a device that's in the EU market for over three years and is actively being used by the clinician.

Now in your definition does it still need to go through this early feasibility? Because when I look at early feasibility guidance document it's really for the device which has low clinical profile.

Owen Faris: I'm sorry. I didn't quite get that last part of your question.

(Neda Moody): Okay. So if the device already is being used in the European market, then does it still need to go through early feasibility study? Because if you look at the early feasibility guidance document...

Owen Faris: Right.

(Neda Moody): ...it is really meant for the device which has absolutely no safety profile.

Owen Faris: So, you know, what we require in terms of IDE requirements for devices that have been studied outside of the U.S. is very device specific. And so it's important to recognize, you know, that many devices are approved in other nationalities with very difference criteria and requirements in terms of what it took to get that device onto the market.

And so when a device has been on the market in, say, Europe and now the sponsor is trying to bring that device through the process in the U.S. we may require many different kinds of things. We may require feasibility data. It may look a lot like early feasibility data.

I agree with you that the early feasibility program is primarily directed to devices that are younger in their development process. But many of these concepts can apply more broadly. We may decide that the data that has been gathered in Europe is sufficient to support a pivotal study without earlier study data being required in the U.S.

In some cases we may decide that the data gathered outside of the U.S. removes the need for any new clinical data to be gathered in the U.S. and we can move directly to a marketing application.

It's really very much dependent on what data were gathered, what the device does, what the risks are, what the potential benefits are. But in some cases and, you know, I did emphasize in my talk that early feasibility doesn't necessarily mean first in human.

In some cases the data that we might require in the U.S., even for a device that's approved outside of the U.S. might look a lot like an early feasibility study. I think Dorothy would like to add some as well.

Dorothy Abel: Yes. I just wanted to emphasize the use of the early feasibility study program is optional. Unlike some other centers, we don't have required stages of clinical study that you have to go through in order to support a marketing application. So you don't have to do an early feasibility before you do a traditional feasibility before you do a pivotal. That's just now how it works.

So you come and you request the level of clinical evaluation that's appropriate based on how final your device design is and the nonclinical information and supportive clinical information you have available to justify initiation of a certain type of study.

(Neda Moody): And the best way of sorting this out would be to interact informally with all of data for reporting I suppose?

Owen Faris: Yes. So the best way to really figure out what is going to be required is to start interacting with that review division. A pre-submission can be very helpful in that process to figure out, you know, you and the review team can figure out how to get to a common point of understanding about what data has been gathered and what data might be needed in order to move a product forward in the U.S.

And again that could result in many different kinds of study and data requirements, depending on many different factors.

(Neda Moody): Okay. Thank you very much.

Coordinator: Our next question is from (Richard).

(Richard): Thank you for taking my question. Would the FDA have a view on single-use devices for clinical trials produced on a pilot or non-fully-validated production line where clearly you can test each device fully prior to use? Would it really be a question of presenting a clinical trial design and risk management file to show that the potential risks had been adequately mitigated in the trial design?

Owen Faris: So many devices that are studied clinically are single-use devices that can't specifically be tested. We look for good processes in place and results of testing that show that you can make a consistent good product.

The kinds of testing we would require are highly dependent again on the kind of device it is, what the risks are that are associated with that device.

(Richard): Thank you. Yes, that's helpful. Thank you very much.

Coordinator: Next question is from (Paul).

(Paul): Hi. I had - I'm trying to figure out how this all applies to my company. I'm a small business and our product has been on the market in the United States for about seven years with no reports of any injuries and it's basically a self-message device.

I'm not even sure it's a medical product, but I'm paying an importer registration and a factory facility cost that's kind of made my product cost increase by about 25%.

So I'm just trying to figure out how, as a small business person, how this applies to me because I get a lot of information and a lot of emails from the

FDA about testing and clinical trials. And I just was wondering what I would need to do or if I need to do anything as far as clinical trials and getting anything approved.

Owen Faris: So I would just say that this is the kind of sort of general question that might be helpful to refer to our - to the email address earlier in the talk. So if you have questions about, you know, what your device, you know, is required in terms of testing and that sort of thing, please send it to that email and then we'll make sure it gets to the right folks.

(Paul): The IDE email?

Owen Faris: Yes. And then we'll forward it on to other folks if we need to.

(Paul): Okay. If I can just have one follow-up question. Is anything being, because I had asked this before actually through my Congressperson, is anything being looked at as far as cost for very small businesses like mine, because clinical trial is obviously expensive but also even just the fees I'm paying, like I say, are very costly to me and actually have made me consider not making the product any more even though it's fairly successful.

Is there any kind of sliding scale or any kind of aid that can be given to small businesses for that?

Owen Faris: So in the context of the IDE process there aren't any user fees or anything associated with the IDE. And so there aren't any costs from the sponsor to FDA. Obviously there are for certain marketing applications but not for the IDE process.

That said we do recognize that some of the questions we ask in the process of reviewing clinical trials have serious impact on sponsors in terms of cost. And while we don't directly consider that as reasons to require or not require certain testing, I think it is an important factor in understanding the impact of the questions we ask and the impact on moving technologies forward.

And so it's something that I think we do want to be thinking about broadly, but not necessarily specifically for a particular sponsor when we're asking certain particular questions.

(Paul): Right. Okay. Well, thank you very much. Thanks for taking my question.

Coordinator: Next question is from (Sandra).

(Sandra): Thank you for taking my question. I wanted to go back to the discussion on submission quality. And one of the items mentioned was that often submissions fail to tell the sponsor's story and that a narrative from the sponsor would be very helpful to FDA on how the sponsor itself interprets the data and why - or their justification on why it's enough.

Would you envision this as, and this is maybe too specific a question, but would you envision this as an executive summary at the beginning of your reports of prior investigation or a more specific paragraph, say at the beginning of each subsection on why your bench testing is enough, why bio compatibility is enough, why animal testing is enough?

Owen Faris: Right. So this is a great question. You know, I think it could - the format of that could take many different forms. But, you know, conceptually it's very similar to what we're talking about in the device evaluation strategy for early feasibility studies.

The concept being that obviously in most cases not every single test that could be done is done in an IDE submission. And there are good reasons for that. And in many cases there are results from certain tests that, seen in isolation, could raise some concerns. But there are often good reasons for why that concern is mitigated elsewhere.

And so looking for a cohesive discussion from a sponsor is really helpful. The early feasibility study guidance specifically lays out one way to do that. Sponsors for other kinds of IDE submissions could consider other ways.

But the thinking is consistent that really hearing how the sponsor views the data and why you think that this is the right amount of testing, these are the right data to support moving forward, is really helpful, because in the absence of that we develop our own story.

You know, we look at the data and we come up with reasons why we might be concerned. And we don't always come up with the same answers for why this shouldn't be concerning that you might.

So it's really helpful to see your argument when we're looking at those data. We still might disagree at the end of the day when our review is complete, but it's really frustrating if it's not in fact a disagreement but a misunderstanding that leads us to a disapproval.

(Sandra): Okay. Thank you.

Coordinator: All right. We have one last question. If you queued up, go ahead and state your name. Please unmute your line. I believe the name was (Commission)?

All right. If you queued up, please unmute your phone and state your question. There are no other questions at this time.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions. Today's presentation along with the slide presentation and transcript will be available in the CDRH learn section of our web site, www.fda.gov/training/cdrhlearn by Friday, January 30, under the tab “How to Market Your Device” in the section titled “Clinical Studies Investigational Device Exemption (IDE)”.

Please note the FDA is not able to provide continuing education credits or certificates of attendance for today's webinar. If you have additional questions about the Medical Device Clinical Trials Program, please use the contact information provided at the end of the slide presentation.

As always, we appreciate your feedback and look forward to your response to our survey. Again, thank you for participating. This concludes today's webinar.

Coordinator: Thank you. This concludes today's conference. You may disconnect at this time.

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