

Webinar: Final Guidance on Patient Preference Information
Moderator: Irene Aihie
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1:00 pm ET

Coordinator: Good afternoon and thank you for standing by, and welcome to today's webinar. All lines are in a listen only mode until the question and answer segment of today's conference. Today, we will be taking questions from the phone lines only. At that time, you may press star one to ask a question. Today's conference is being recorded. If you have any objections you may disconnect at this time. I would now like to turn today's conference over to Ms. Irene Aihie. Thank you. You may begin.

Irene Aihie: Thank you. Hello, and welcome to today's FDA webinar. I am Irene Aihie of CDRH's Office of Communication and Education. On August 23, 2016, the U.S. Food and Drug Administration published the final guidance document, patient preference information, voluntary submission, review, and PMAs, HDE application, and de novo requests, and inclusion in decision summaries in device labeling, which outlines recommendations on patient preference studies that may result in valid scientific evidence and how stakeholders, including industry and patient advocacy organizations, can voluntarily collect and submit through FDA patient preference information.

The focus of today's webinar is to share the information and answer questions about the final guidance document. Today's presenters are Annie Saha,

Director of External Expertise and Partnerships in the Office of the Center Director and Martin Ho, Associate Director for Quantitative Innovation in the Office of Surveillance and Biometrics here in CDRH. Following the presentation, we will open the line for your questions related to topic in the final guidance only.

Additionally, there are other subject matter experts available to assist in the Q&A portion of our webinar. Now, I give you Annie.

Annie Saha: Thank you, Irene, and good afternoon everyone. For sake of brevity, I will refer to the guidance as just the patient preference guidance and not the full title for the rest of the presentation. And the agenda for this webinar is really to provide some context and overview of the patient preference information final guidance as well as describing some key updates to the benefit risk worksheet in the factors to consider when making benefit risk determinations in medical device premarket approval and de novo classifications guidance that was originally issued in 2012. And then as Irene noted, we will follow-up with question and answers.

So a bit of context and scope as to really how we get where we are in terms of the patient preference initiative and the guidance development. We're really seeing in the larger healthcare ecosystem the evolution of the role of the patient where in the traditional medicine sort of field where the provider has really led the treatment decision making, patients follow the instructions of their providers, into the late '80s when -- into the '90s when HIV/AIDS, cancer patient advocacy groups really banded together to ask for access and availability to new treatments.

And then with the internet, patients really became empowered through all the information that was then available to them and in the future, which is where

we are today, is that patients and providers are really in a partnership where they're really able to work together and determine what's the best treatment decision and make that decision for themselves. And patient preferences can really help us inform the regulatory decision making and that role has evolved internally as well.

So we issued -- this really started -- our first stake in the ground was in 2012 with our updated guidance. Now, in 2016 where we really stake out what are the factors that should be considered when making a benefit risk assessment and that one factor that is key and of importance is really what patient's perspectives are on both the risks and their perspective on benefit, understanding that different patients are going to have different risk tolerances and that's going to vary, and it may reveal that different participants are willing to tolerate a different level of risk to achieve a probable benefit, and that patients are the ones who are uniquely qualified to give us that information and help us balance our benefit risk assessments with that information, along with other clinical and non-clinical data.

This led to our strategic priority for 2016-2017 where we really recognized that patients -- we really need to partner with patients and we really must interact with them as partners to really advance development and evaluation of innovative medical devices. And this strategic priority really has two prongs. One is to promote a culture of meaningful patient engagement by facilitating interaction between our staff and patients, and then increasing the use of transparency of that patient input as evidence in our decision making processes. And that's really where the focus of the patient preference guidance and this discussion will be about.

Overall, we see that patient information could really come to us in a variety of ways and patient input is really that broad umbrella of the types of

information that FDA receives in terms of the perspectives of patients, anything from anecdotal comments and correspondences to FDA, testimonies at advisory committee meetings, opinions that are expressed via social media, as well as surveys and even -- and then the more quantitative measurements of patient reported outcomes, patient preferences, et cetera. And then a subset of that information is really patient perspectives, which is really a type of patient input and that's really information that's really relating to the patient's experience with a disease or condition and how they manage that condition.

And this is really useful for both understanding the disease and having a better understanding of that impact on patients, identifying what outcomes are most important to patients, and then really understanding what are those benefit risk tradeoffs for treatment that are important to patients. So patient input is kind of the house if you will and then the two-car garage, patient perspective, is both your patient preference information and then your patient reported outcomes.

So what is patient preference information? So for the purposes of this guidance, we refer to patient preference information as the qualitative or quantitative assessments of the relative desirability or accessibility to patients as specified alternatives or choices among outcomes or other attributes that differ among alternative health interventions. And it's also important to note that when we use the term patients, we are -- would also include ideas like -- include care partners, such as parents who are in the pediatric population or potentially the children of elderly patients maybe who have dementia, et cetera, and healthcare professional preferences could also be taken into account.

So what can patient preference information provide and how can it be used? So the patient preferences can really provide us with valuable information

about what are the benefits and the risks that are most important to the effective patient population, what are the benefit risk tradeoffs that are acceptable from a patient perspective. So what benefits are patients willing to take in exchange for certain risks and how do patients really think about those tradeoffs? And then are there relevant subgroups of patients that would really accept a particular benefit risk profile or choose a potential treatment option over other alternatives that exist.

Various potential uses for patient preference information could include informing both end points for (effect) size, for clinical studies, as well as informing subgroup considerations. Patient preference information could ultimately also impact the labelling changes or expanded indications. Areas where patient preference information could be used outside a regulatory context could certainly include areas such as shared medical decision making.

What's the difference between patient preference information and patient reported outcomes? And this is a question we get quite a bit so we want to try to explain what -- the differences there are. So patient reported outcomes is really a report of the status of a patient's health condition that comes directly from the patient without any interpretation from -- of the patient's response by a clinician or anyone else. And these instruments are really designed to measure a patient's perceptions of health status before, during, or after therapy.

So for example, a patient reported outcome might be related to pain and so clinicians will ask patients for how they're feeling both before treatment, during the treatment, then after a therapy whereas patient preference information, patient preference studies really study what specified type of therapy or attributes of a given product a patient might prefer. So if we continue with the pain example, it might be what is the level of pain you're

willing -- that you would like to be reduced for you to accept a certain risk. So it's about that trade off and about what those different attributes are versus the health state.

Now, we'll go into an overview of the guidance itself and kind of highlight the objectives, the scope, and the various sections of the guidance. So the overall objectives of the guidance are to encourage submission of patient preference information, if available, whether by sponsors or other stakeholders to submit that information to FDA to aid in our regulatory decision making. We then go into outlining the recommended qualities of those patient preference studies, which then may be result in valid scientific evidence, and then to provide recommendations for collecting and submitting that information, as well as discussing how patient preference information will be included in our decision summaries and provide recommendations for the inclusion of that information in labeling.

The scope, really, is explaining the concepts of the guidance that sponsors or other stakeholders should consider when choosing to collect patient information, which may effect and inform our benefit risk determinations for pre-market review of PMA devices, HDEs, as well as de novo requests, as well as discussing the inclusion in terms of how we'd be transparent about the use of that information.

I want to be clear, though, patient preference information submission to FDA is voluntary and there are certainly cases in device areas where patient preference information may not be relevant or appropriate. Certainly, we see that it's useful for sponsors to essentially collect or submit this information when the usage decisions by patients and the healthcare professionals are preference sensitive. So the idea there being that there might not be a gold standard of treatment or there's variable evidence about the different benefits

and risks of different types of treatment that exist. Or there's different -- there's heterogeneity within the patient population and different patients are going to have different decisions about which type of device, or drug, or, you know, whether to have surgery for treatment.

So really the devices that could benefit from patient preference information are those with characteristics like a direct patient interface, devices that could yield significant health or appearance benefits that are directly related to quality of life, certain lifesaving but high risk devices, devices that really are developed to fulfil an unmet medical need or treat a rare disease or condition offer some kind of alternative benefits to something that's already on the market are areas where there's a novel technology and the benefits and risks aren't necessarily well known or understood.

I will now turn it over to Martin Ho to discuss about how patient preference information uses valid scientific evidence.

Martin Ho: Thank you very much, Annie. FDA respect and appreciate input from patients. Therefore, we evaluate submitted patient preference information as valid scientific evidence along with other evidence from clinical and non-clinical testing when making benefit risk determinations. The guidance will not change any review standards for safety or effectiveness. The patient preference information evidence provides additional insights from patient for benefit risk assessment. The guidance provides recommendation regarding the voluntary collection of patient preference information that may be submitted for considerations as valid scientific evidence as part of the FDA's benefits assessment.

Well designed and conducted patient preference study can provide valid scientific evidence regarding patient's risk tolerance and perspective on

benefit. This may inform our evaluation of a device benefit risk profile during the PMA, HDE application and de novo request review processes. The guidance has listed 11 recommended qualities of preference studies. While there are different ways to group these qualities, for the purpose of this presentation we organize them in three different domains.

They are: all about patients, good study design, and good study conduct and analysis. Next, we will discuss individual qualities. First and foremost, patient preference studies should be patient focused. If feasible, studies should primarily measure the preferences and perspective of well-informed patients, not other people or their physicians. This study should use a representative sample of adequate size so that the study result can be reasonably generalized to the population of interest. The patient's benefit risk tradeoff preferences may be heterogeneous even among those with the same disease or condition. So therefore, studies should reflect the preferences of patients from the full spectrum of disease for which the device is intended to be used.

Finally, study participants should understand the harm, risk, benefit, uncertainty, and other medical information being communicated to them. The second domain of recommended qualities is good study design. A study design determines the qualities of a patient preference study because it specifies what the study measures and how to measure them. In general, quality of a study may be established if it follows guidelines for good research practices established by a recognized professional organization. Effective communication of benefit harm, risk, and uncertainty can reduce uncertainty caused by misunderstanding. For example, we will opt for multiple formats of presenting of probabilities because different format may work for different patients. We also highly recommend conducting pretests of the communication format or survey instrument to make sure the respondents understand of the questions.

It is very important for us to minimize cognitive biases such as framing, anchoring, simplifying heuristics, or order effects. And in order to collect relevant evidence to inform regulatory decision making, it is very important that the sponsors come talk to the FDA at early design stage. At that time, we can discuss relevant harm, risk, benefit, and uncertainties included in the studies. We may also want to maintain some level of consistency among the benefits, harm, risk, and other attributes between the patient preference studies and the clinical evidence.

Finally, it's also very important that the relevance of a specific endpoint to potential clinical outcomes be clearly communicated to patients who convey their preferences.

Implementation and good study design are both equally important for a valid scientific study. So the third domain of recommended qualities is good study design and good study conduct and analysis. Just like a valid clinical study, compliance of research staff and study participants with the study protocol determines the scientific integrity of the study. If feasible, study analysis plans should include some types of consistent checks, consistency checks such as internal validity test of logic and consistency. Finally, robustness of analysis results can be evaluated by identifying the potential sources of uncertainty in conducting sensitivity analysis as specified in the studies analysis plan.

There are some regulatory considerations regarding submissions of patient preferences information for studies submitted with other pre-market review data, applicable regulations including IDE regulations in (21 CFR Part 812) must be valued. For studies done independent from a device clinical study, FDA generally considers the study to be non-significant risk. Conditions of approval may be applied in some cases. FDA may impose conditions of approval in certain PMA approvals including where the agency take the

patient preference information into account to mitigate risk and facilitate use in patients for whom benefits are expected to outweigh risk.

FDA may also require collections of post-market evidence through a post-market approval surveillance studies for the PMAs. As I said, FDA encourages sponsors and other stakeholders to have early interactions with the relevant FDA review divisions if they're considering collecting and submitting patient preference information. You can request an information (unintelligible) submission meeting with us to discuss plans for designing and submitting patient preference studies. Annie and I provided our email addresses here so that you can request our participation in your interaction.

Next, I'm turning to Annie.

Annie Saha: So we've also in the guidance outlined how the inclusion of patient preference information may be included in both our decision summaries as well as potentially in device labelling. So when we do consider a patient preference study in our premarket submissions, we generally will include that in the decision summary. And as part of our strategy priority efforts for 2016-2017, we have already started this and will be continuing to do so. The inclusion of this information we feel is going to be helpful for both healthcare professionals and patients in terms of making their decisions, especially in areas where there are difficult benefit-risk tradeoffs are novel treatments.

And additionally, patient preference information that's reviewed by FDA and supports an approval or marketing authorization should also be described in the device labeling, and that that labeling should contain sufficient information about the benefits and risks of the treatment for diagnostic options under consideration. And certainly, please see our final guidance about device labeling for additional information. We also provide here some examples and

some resources for you to use if you're considering doing a patient preference study.

CDRH embarked on our sort of proof of concept study on how we could use patient preferences in obesity and the citation for the paper, which outlines how that information was then incorporated as evidence in our regulatory decision making, is included here for your -- for you to take a look at and was published in Surgical Endoscopy. We also have the benefit risk guidance -- the factors to consider for benefit risk determinations and pre-market approvals of de novo classifications as well as guidance on medical device patient labeling and through collaboration on the science side -- regulatory science side -- we worked with the Medical Device Innovation Consortium on their patient centered benefit risk project, where they have a framework for how patient preference information could really be incorporated across the device lifecycle, as well as a catalog of methodologies. And they've recently also just published a resources for sponsors with some frequently asked questions and their website for MDIC and the resources there are listed as well.

And finally, we'd like to give you an update on the benefit risk -- the summary changes to the benefit risk pre-market guidance and some updates we made to the benefit risk worksheet. Overall, we updated the guidance to ensure consistency with the terminology and the concepts in the patient preference guidance. And with that, in section four of the guidance, we talk about the factors FDA considers when making benefit risk determinations and really added some additional information and clarity about those additional factors and the assessment of the probable benefits and risks of devices.

We also included the addition of patient preference information and fleshed that out more in the benefit risk worksheet that FDA staff uses to guide benefit

risk determinations of PMA and de novo requests, including the section on patient perspective on risks and benefit. And to note both the patient preference guidance and the benefit risk guidance have a 60-day implementation period from the date of publication.

So in summary, patient preference information is voluntary. It can be informative during the benefit risk assessment. As Martin noted, this doesn't change any of our standards for safety or effectiveness and that also, patient preference information can really be informative earlier at device assessment and appendix A of the guidance has sort of a flow diagram of where patient preference information can be incorporated and how it could be used, all the way from discovery, device design into clinical study parameters such as endpoint selection, or effect size. And again, we really would like to encourage early interactions with the FDA staff if you are interested in planning, or designing, or submitting a patient preference study. And Martin and I are available to -- via email or to discuss both a potential study or be part of those review meetings.

With that, I'd like to thank you for your time and we'll open it up for questions.

Coordinator: Thank you. At this time, if you do any have any questions or comments, you may press star followed by the number 1. Again, that is star 1 to ask a question. Please unmute your phones and state your first and last name when prompted. One moment please.

(Mike McGurty) joined - has a question.

(Mike McGurty) Hi, thanks for taking the question. Regarding the 60 day date of applicability, is that for entirely new applications or would it apply to applications that are already in process?

Annie Saha: So this would be for new applications and so the effective date is October 23.

(Mike McGurty) All right, thanks very much.

Annie Saha: And again, it's voluntary so it's not a requirement of sponsors to submit a patient preference study as part of their submission.

(Mike McGurty) Okay. Just to follow onto that, is this something where trying to incorporate PPI into an application that's already in process, are the reviewers at ODE going to think that maybe the whole package needs to be rewritten or can you attach this sort of thing in a modular fashion to a PMA, for instance, that's already in progress.

Annie Saha: It could be attached as a modular to a PMA that's already in progress.

(Mike McGurty) Okay. Thank you very much.

Coordinator: Thank you. Once again, if you do have any questions or comments, you may press star one. Karen Jaffey, you may ask your questions.

Karen Jaffey: Yes, hi. I had a question with regards to extending this preference type of assessment to a user, so if it's a prescription device, the actual -- there's the patient preference information but then there's also the physician as a user of the device itself. Is that something that you see in the future? Is that something that's going to be extended by this guidance? What are your thoughts there?

Annie Saha: In our definition of patient preferences, we do include if there is a healthcare professional sort of preference that could be considered as part of the package or as part of a patient preference study.

Karen Jaffey: And so that would be something that you could collect in the same fashion that you described during the seminar here as far as gathering that data and the information and so forth?

Martin Ho: Yes, I think the same criteria applies.

Karen Jaffey: Okay. But it could not -- it should not be an endpoint, as an example though, in a study?

Annie Saha: I don't foresee a scenario where that would be the case, but certainly something to come in and talk to us about.

Karen Jaffey: Perfect. Thank you.

Katie O'Callaghan: Katie O'Callaghan - I'm the CDRH assistance director for strategic programs and I have the honor and privilege of overseeing this partner (unintelligible) this guidance. I just wanted to expand on that. The patient preference work could potentially be used to support justification for selection of a given endpoint out of a list of potential endpoints. And in addition to that, could also be used as part of the justification to support a given effect size that would be considered clinically meaningful.

Karen Jaffey: That's helpful. Thank you.

Coordinator: Thank you. (Yasmin Sakhel), you may go ahead.

(Yasmin Sakhet): Hi, good afternoon. Thank you for this presentation. We're from (Accivent) and we have a quick question. We understand about the patient reported outcomes guidance, but we were interested in learning whether or not the patient preference guidance can be applied to small molecules of biologics.

Annie Saha: So the Center for Biologics did sign onto this guidance specifically if the submission is related to PMA and de novo requests or HDE applications. So it's specific to those -- to that application type. Certainly, feel free to reach out to the Center for Biologics if you have additional questions in other areas where they might be interested in looking at preferences.

(Yasmin Sakhet): How about some small molecules? Any other similar guidance that we can refer to?

Annie Saha: I would, again, follow-up with the Center for Biologic Evaluation, Research, and they can discuss with you how to incorporate the patient voice in small molecules, molecular,.

(Yasmin Sakhet): Okay. Thank you.

Coordinator: Thank you. Once again, if you do have any questions or comments you may press star one. At this time, I am showing no further questions. One moment please. Julie Lesley, you may go ahead.

Julie Lesley: Yes, what are your thoughts on including something like a question on net promoter value where after a patient or a physician goes through a clinical trial, you ask them if they -- what would be their chances of recommending this device to others? Would you consider that information?

Martin Ho: Yes. I think it's a very meaningful question to collect a (unintelligible) and (unintelligible) the clinical trials. But it's -- in terms of the nature of the data, it's different from the patient preferences information that we have been presenting.

Julie Lesley: Thank you.

Coordinator: Thank you. (Richard Counts) you may go ahead.

(Richard Counts): Yes, I was just wondering if it's a -- if it's a good idea to talk to FDA before conducting this patient preference and whether it's required given that many times these patient preference surveys are given to patients who are not yet being treated since there's no -- I can't see any risk to the patient. So I guess my question is it necessary -- is it good to talk to FDA beforehand and is it required?

Annie Saha: We certainly recommend if you're interested in conducting or performing a patient preference study to come talk to us early and we would be happy to do so. In terms of requirement, it is not a requirement. The submission of patient preference information is voluntary.

(Richard Counts): Thank you.

Coordinator: Thank you.

Martin Ho: Yes, I just wanted to expand on that in these sense that when coming to talk to us, you not only be -- help us and understand your design better and so that you end up with a better study. But also it's more important that the result of the study can yield data that can support and inform our regulatory decision

making. But this is a critical point so as Annie said, come early please.

Thanks.

Coordinator: And would you like to go to the next question?

Irene Aihie: Yes, please.

Coordinator: Thank you. CDRX, you may ask your question.

(Dean Brundang): Yes, this is (Dean Brundang). A question regarding the recognized professional organizations from the webinar today. Does FDA have a list of those that would be considered FDA recognized to do this type of work?

Annie Saha: We do not endorse anyone to do patient preference studies. There are other groups that certainly are doing work in terms of methods and potentially standards development for patient preference studies but that is not something the FDA will do or be involved in.

(Dean Brundang): Thank you. Heather Nagel, you may go ahead.

Heather Nagel: Thank you. I'm just curious approximately how many patient preference studies have contributed to either a clearance or approval to date. I'm wondering if this is an increasing trend in the industry or if this is a relatively new concept still?

Katie O'Callaghan: This is Katie O'Callaghan. Thanks for your question. The use of patient perspectives is certainly an increasing trend across the healthcare space and certainly within the device and other medical product industries. The use of quantitative patient preference studies are relatively more rare. We are seeing an increase in that. We expect to see a continued increase in that with the

finalization of this guidance in this policy, but certainly the inclusion of patient perspectives and other forms of patient input is quite a growing trend across the medical product space.

And so if folks have any interest in speaking with the FDA about other forms of patient input outside the scope of this guidance, we would be happy to follow-up after this webinar and you can direct those questions to the email that's on the screen.

We'll take our next question.

Coordinator: Thank you. Jose Cabrera, you may go ahead.

Jose Cabrera: Hi, thanks for the talk. So far very interesting. The concept of usability studies has been around for a while and essentially been standardized in pre-market applications to the FDA. It seems like if the user is the patient it would be plausible to be able to integrate some of these patient preference concepts into currently standardized usability studies. Would you guys agree with that more or less?

Martin Ho: I would say that the focus of the studies for user feasibility study in a patient preferences are different. Feasibility studies may need to (unintelligible) to determine whether some features that are user friendly or whether it's something that could be improved upon the interface so that the machines or devices can be correctly used. Versus patient preference studies, they are studying the preferences among different attributes or benefit risk profiles between different (unintelligible) options. So it's about the tradeoff between benefits, risks, and other (unintelligible) treatments.

Jose Cabrera: Okay. Thanks.

Coordinator: Thank. (Ron Schoengold) you may ask your question.

(Ron Schoengold): Yes, is it possible to apply the principles of PPI to a traditional 510K?

Annie Saha: So the scope of this guidance is, of course, pre-market PMAS, de novos, and HDE requests. But, you know, contact the review division or contact Martin and I if you have questions about usability or generalized ability to a 510K.

(Ron Schoengold): Right, this is an incidence where a direct patient interface is required with a medical professional. So it's a little bit -- not just a straight device submission.

Annie Saha: Okay. Well, feel free to reach out to us or also to DICE, dice@fda.hhs.gov for additional questions or follow-up.

(Ron Schoengold): Thank you.

Coordinator: Thank you. Once again, if you do have any questions you may press star followed by the number one. (Mac McKean), you may go ahead.

(Mac McKean): Thank you. Thank you for this call. Very informative. Regarding the PPO, industry, particularly in the implantables cardiac space have in the past used quality of life surveys and on occasion there are validated instruments such as hall walks. Do you see a PPO in this type of a design being similar to a quality of life endpoint?

Martin Ho: I think by PPO you mean PRO, correct?

(Mac McKean): Right, Patient Reported Outcome, correct.

Martin Ho: Yes, can you repeat the question? I'm sorry?

(Mac McKean): Well, just aligning the PLL with a quality of life survey that (unintelligible) industries conducted on certain implantables such as a hall walk. And in some cases there was quality of life surveys become validated instruments to be used in clinical trials. How would you compare that to a PRO?

Annie Saha: So quality of life measures you discuss like this six minute walk test, it would be a patient reported outcome and we do have guidance about patient reported outcomes and how they could be validated. I just pulled up the slide where discuss kind of what the difference is between a patient preference study and a patient reported outcome. So what you mentioned was really a patient reported outcome in terms of the health status from the patient directly about how they're doing versus a patient preference study, which is really about the types of attributes or in terms of the benefit risks where that patients would prefer. And primarily, they wouldn't have even had the treatment at that point.

(Mac McKean): Thank you.

Katie O'Callaghan: Other interesting potential intersection point between patient preference and patient reported outcomes is that it's the one we're interested in using patient preference methods to obtain a better understanding of what's most important to the patient out of a list of potential outcomes and one or more of those potential outcomes is a PRO. That would be potentially highly informative, particularly in areas for which there are either novel technologies being developed and so the regulatory framework is still evolving along with that technology development, or in areas where we're seeing novel features or other changes being made to an existing technology, which may change

patients' views on what is important to them and how they would value those various attributes alongside the benefit and risk that's offered.

Martin Ho: Another interesting (unintelligible) between PRO and PPI is that for a subtype of PRO that's called preference based patient reported outcomes, they evaluate general health states into various different health status. And for each status, they link with something called (unintelligible). So that is -- perhaps I digress a little bit, but this is a possibility that we can link both together.

Coordinator: Thank you. And once again, if you would like to ask a question or have any comments you may press star one. Again, that is star one to ask a question. One moment please. (Unintelligible) you may ask your question.

(Linda): Hi, this is (Linda) from (Yansen). I had a question related to geography of conducted PPI studies. Is the assumption that the patient population is strictly U.S.?

Annie Saha: Primarily (unintelligible) information -- patient preference information could be elicited, whether in the U.S. or abroad -- but if you were to use any OUS data or any OUS patient preference studies that would have to conform to other guidances that we have about the use of outside the U.S. studies. So same policy as any other outside the U.S. data.

(Linda): Thank you.

Coordinator: Thank you. At this time, we are showing no further questions. I'd now like to turn the call back over to Ms. Irene Aihie for any closing comments.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions. Today's presentation and transcript will be made

available on the CDRH Learn webpage at www.fda.gov/training/cdrhlearn by Wednesday, October 5. If you have additional questions about the final guidance, please use the contact information provided at the end of the slide presentation. And as always, we do appreciate your feedback.

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

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

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