

NWX-FDA OC

**Moderator: Irene Aihie
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1:00 pm CT**

Coordinator: Welcome and thank you all for standing by. At this time all parties are in a listen-only mode until today's question and answer session.

Throughout this conference questions will only be taken via the phone lines. If you do have a question you can press Star 1.

I would like to inform all parties this conference is being recorded if for any reason you object to that you may disconnect at this time.

I'll now turn the conference over to Irene Aihie. Ms. Aihie 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 January 21, 2016 the US Food and Drug Administration issued the final version of the guidance document Submission and Review of Sterility Information and Premarket Notification 510(k) Submission for Devices Labeled as Sterile.

This guidance seeks to ensure that manufacturers incorporate adequate sterilization methods for 510(k) devices labeled as sterile and provide appropriate documentation and information to the FDA for premarket review for established and novel sterilization processes.

The final guidance also provides additional details about the pyrogenicity testing information that sponsors should include in a 510(k) submission.

The focus of today's Webinar is to review the document and help manufacturers and other stakeholders understand the information provided in this final guidance.

Your presenter is Steven Turtill, a biologist from the Office of Device Evaluation.

Following the presentation we will open the lines for your questions related to the topics in this guidance only.

Additionally there are other center subject matter experts available to assist with this Q&A portion of our Webinar. Now I give you Steven.

Steven Turtill: Well good afternoon everybody. Welcome and thank you for joining us this afternoon.

My name's Steven Turtill. I'm a biologist in the Division of Orthopedic Devices. And the subject of today's Webinar is the new guidance Submission and Review of Sterility Information and Premarket Notification Submissions for Devices Labeled as Sterile.

This was issued on January 21 but I want to bring immediately to your attention that there is a 60 day delayed implementation period.

This is to allow industry to prepare prospective submissions, to allow for completion of 510(k) submissions currently under review, and to allow for training of FDA review staff on new device guidance and review procedures. So this will be fully implemented on March 21, 2016.

And to provide a little bit more guidance on the middle bullet, that means that all new submissions received on or after March 21 will be subject to the new guidance document.

So this is an outline of the Webinar. We're going to go into the background a little bit, talk about the scope, what's included and what's not, talk about the sterilization method categories, and information to be included in submissions.

Taking a look at the background, going back to 1990 the very first guidance that was published on this issue was the K90-1. That was published to bring greater consistency to review processes across all divisions and product classes.

In 2002 this was updated. And this update was issued to address several significant changes that have occurred in the regulatory environment including FDAMA in particular.

In 2008 a draft was proposed to address advances in sterilization technology, provide clear definitions for novel sterilization methods, as well as update the guidance related to pyrogenicity claims.

And finally in 2016 the final was published. And this was a revision that was intended to provide public comment resolution for the 2008 draft, which provides clarification of the scope, clear definition of the novel sterilization methods, and additional guidance related to the pyrogenicity issues.

So all of these - each of these steps were provided to ensure greater 510(k) review consistency.

One item I'd like to add here is that during the public comment resolution period we actually received public comments from a good number of sources including device manufacturers, contract sterilizers, test labs, and a trade association.

The scope of this guidance is limited to the review of 510(k)'s for devices labeled as sterile that are subject to industrial terminal sterilization processes based on microbial inactivation.

Taking a look at the exclusions from the 2008 draft; outside the scope of the guidance document are processes that rely on microbial exclusion rather than microbial inactivation. Examples of those are filtration and aseptic processing.

The other exclusions include processes intended to be to sterilize medical devices that incorporate materials of animal origin, process intended to be used by reprocessors of single-use devices: there is a separate guidance document for that. And information on cleaning, disinfection and sterilization of reusable devices that are reprocessed in healthcare facilities.

There's also a separate dedicated guidance document for that which was actually updated about one year ago.

So this is from the 2008 draft. And based on public comment resolution we actually wound up adding two additional exclusions that includes Item Number 1 and Number 4; sterilizers that are themselves medical devices subject to 510(k) review. And it excludes processes that incorporate the use of liquid chemicals sterilants.

So moving on to Roman Numeral IV, methods of sterilization, you may recognize these methods from earlier versions of the guidance document -- traditional sterilization methods, non-traditional sterilization methods and novel non-traditional sterilization methods. And in the 2008 draft there was another section that followed it which included examples of each.

Moving up to the 2016 final version these are different; now the nomenclature has changed. Now we're looking at Established Category A, Established Category B, and Novel sterilization methods. And integrated into each section are examples of each sterilization method.

So taking a closer look Established Category A methods. These are methods that have a long history of safe and effective use as demonstrated by ample literature, clearances of 510(k)s or approvals of PMAs, satisfactory quality system inspections. And FDA-recognized consensus standards for development and validation and routine control.

Examples of these include dry heat, ethylene oxide in fixed rigid chambers, moist heat also known as steam, and radiation; examples include gamma and electron beam radiation.

Taking a look at Established Category B, these are methods for which there are no FDA-recognized dedicated consensus standards.

There is published information on development validation and routine control. And FDA has previously evaluated sterilization development, validation data for specific sterilizers using discrete cycle parameters and determined the validation methods to be adequate.

Examples of Establish Category B are hydrogen peroxide, ozone, and flexible bag systems.

And the third category is Novel sterilization methods. These are newly developed methods for which there is little or no published information, no history of comprehensive FDA evaluation of sterilization development and validation data through an FDA clearance or a PMA approval for the devices that are subjected to these sterilization methods, and no FDA recognized dedicated consensus standards on development validation and routine control.

FDA has not reviewed and determined these methods to be adequate to effectively sterilize the device.

Examples of these include vaporized peracetic acid, high intensity light or pulse light, microwave radiation, sound waves and ultraviolet light.

So this is the key message throughout the guidance document. Evaluation by FDA of validation data where; the specific process has not been evaluated by FDA because the parameters of an FDA cleared sterilizer had been altered, or because the validation data have just not been evaluated based on submission on a particular submission, we consider these methods to be Novel.

And the underlying theme here is that it's important for us, were looking for a high degree of assurance that each method has been adequately validated.

And whether that means we're looking at conforming to standards or based on information we've already received, we want to know that the validation has been performed adequately.

And in the instance of Novel sterilization methods, we're going to be looking for the validation data for the first time.

So that leads us as a natural segue, actually, into the sterilization methods, which is Roman Numeral V of the guidance document: Sterilization Information for Devices Labeled as Sterile.

So this goes back to 1990. This is the very first guidance document that was issued.

And we're looking back, then we we're looking at the number of items to help us have assurance that the validation has been conducted effectively, and for some other basic information about the submission.

These include the sterilization method, the method used to validate the sterilization cycle, the sterility assurance level, the description of the packaging that is designed to maintain the product's sterility.

If the sterilization involves ethylene oxide, then the ethylene oxide residuals. And if the device is labeled pyrogen-free, we're looking at the method to make that determination.

And finally if the sterilization method is radiation, we're looking for the radiation dose. This is what we were looking for in 1990.

I'm going to highlight a couple of these things, and these include the sterilization method, the radiation dose if radiation was used, and residuals of ethylene oxide if ethylene oxide was used.

Just moving forward 12 years to 2002; the same information we're looking for, including the sterilization method. (We have a little bit of misalignment here. Sorry about that.) We're looking for the radiation dose if radiation was used, and also ethylene oxide residuals if ethylene oxide was used.

Moving forward to the 2008 draft guidance, we're looking at the sterilization method again, the radiation dose, and sterilant residuals.

In the 2008 version we actually reorganized it, presented these upfront so they're - because it just told a little bit better story. And in most applications we see these things straight up front and it makes it a little bit easier for the reviewers as well.

Also instead of just stating the ethylene oxide residuals we expanded what we were looking for. We used the expression "sterilant residuals" instead of just ethylene oxide, because we know now there are other chemical sterilization methods.

So taking that format and moving it up to 2016, again we're looking for the sterilization method, the radiation dose if radiation was used, and the sterilant residuals depending upon what the sterilant is.

So what looks different here from the 2008 version is that there's a whole new block of text right in the middle of the page, and this is Section B, C, and D. So it's time for a closer look at that.

And I want to bring it up and remind you that again; where the specific process has not been evaluated by FDA we're interested in taking a closer look at that. We consider those methods to be novel and this is part of the first step in identifying exactly which category of sterilization methods the process belongs to.

So we've added Part B, C and D and taking a closer look at those; a description - just a description - of the sterilization chamber if it's not rigid or fixed.

We're also looking for information on Established Category B. If the sterilizers receive a 510(k) clearance, then we would like to see the 510(k) number included in the submissions, as well as the make and model of the sterilizer.

Finally we would like to see information related to whether or not the cycles were altered. If the sterilizer had not received 510(k) clearance, that should be stated in the application.

And if the sterilization method has been evaluated through clearance of a 510(k), or approval of a PMA, we'd like to see a submission number and the device master file number.

If the cycle has changed since those clearances or approvals, we also want to know if the cycle's been altered.

And lastly, we're taken a look at the sterilization sites, in other words we want to know the actual address of the sterilization facility.

All this - all of this information will help us get confirmation or make the determination whether this is an Established B or a Novel method, in particular.

So moving on to Item Number 2, the 2008 draft; we're looking for a description of the method used to validate the sterilization cycle but not the validation data itself.

And we expanded this to ask you to identify all relevant consensus standards. In Item Number 3 we're looking for the sterility assurance level.

And when we move up to 2016 version, the final version; we're asking for a description of the methods used to validate the sterilization cycle, not the validation data but all relevant consensus standards, and in the absence of recognized standards, a comprehensive description of the process and a complete validation protocol.

Item Number 3 is we're looking for the sterility assurance level and that really hasn't changed. We've just provided a little bit more guidance.

Looking back to the 2002 version and earlier Item Number 4 is the pyrogenicity issue. If product is labeled as pyrogen free, the description of the method used to make that determination; for example a *limulus* amoebocyte lysate test.

So moving to 2008 we're asking for the same information but we've provided more guidance and been a little bit more prescriptive about which devices we're looking for this information on. That's pyrogenicity testing. And that includes; all blood contacting devices, implants, devices that contact cerebral spinal fluid, and devices labeled pyrogen free or non-pyrogenic.

We've also expanded information that we're looking for with regard to the testing itself; identification testing endpoint, explanation supporting the selected endpoint. And, at the bottom of that slide we also provide some information on additional guidance and references.

So moving up to 2016, you'll note the color coding. We're still looking for - we're providing prescriptive information about which devices we'd like to see pyrogenicity test information on.

And the next block of text down, we're looking for a description of the method used to make the determination, identification of the chosen test limit, an explanation supporting the selected test limit. But we're also looking for - and the number - the amount of endotoxins, endotoxin units per device.

And in addition we're looking for statement confirming that endotoxin testing will be conducted on every batch, or if not, we're looking for a sampling plan and a justification for that.

And finally again at the bottom are several references. But these have been updated to make them more current.

So the USP General Chapter <161> has been updated to the 2015 version. The AAMI ST72 has been updated to 2011.

And the 2012 release of the guidance "Pyrogens and Endotoxins Testing: Questions and Answers" from the FDA was issued and replaced the 1987 LAL testing guidance guideline from the FDA which has been withdrawn.

So an additional note on that, we received a lot of reviewer comment. I'm just going to move back one slide.

We did receive a lot of comment with regard to the pyrogenicity testing. We had a number of comments that were saying this was too prescriptive. And we also had a number of comments that said that this was a good thing. We're being more consistent with, for example AAMI ST72, which is FDA-recognize, and which does call for this information.

Since that time both the other two references that are listed there have all harmonized, so all publications right now, the three listed there including the current guidance that we're talking about, are all harmonized on these issues.

And the final item in 2008, we're looking at the description of the packaging but not the packaged data itself. And this is the packaging that's designed to maintain the device's sterility.

And when you move ahead to 2016, we're looking at a description of the package that's designed to maintain the device's sterility, but not the package test data, and the description of the package test methods.

So we want a summary here of exactly what sort of simulations were conducted and what sort of testing was done. For example, what sort of accelerated aging may have been conducted and how that was followed by seal strength testing, and what sort of simulated shipping and handling was conducted and what sort of package integrity was conducted after that.

One additional note on this is there are exceptions; there are for some devices reviewed by some divisions that do want to see package test data for certain expiration dating. And we encourage you to be in contact with the division

that reviews your particular device type to find out if you need to provide that information as well.

So moving on, we're about to jump into the very last section which is the Novel sterilization methods. But before doing that I would like to revisit some text from earlier slides. This is for Established methods. And we've already seen this. This is excerpted from two different earlier slides.

For established Method A and B we're looking for a description of the sterilization method and a description of the method used to validate the sterilization cycle, all relevant consensus standards, and in the absence of recognized standards a comprehensive description of the process and the complete validation protocol.

So moving ahead and taking a look at the Novel methods, you'll notice right off and the first thing we're looking for this is in addition to all of the information we've just discussed, everything that's documented in Section 5 above, we want to see that information but in addition we're looking for a comprehensive description of the sterilization process. So we really want to look at the details.

Of course what we're starting with here is, we want to look at all of the validation information that we haven't seen before, so a comprehensive description of the methods is what we're looking for to start off with.

A method used to validate the sterilization cycle, the validation protocol, as well as the validation data for the process.

FDA may also request additional information based on the specific device submitted for review.

And this slide really just summarizes all the content changes from 2008 to 2016. This includes clarification of the nomenclature change.

The previous version included Traditional Non-traditional and Novel non-traditional methods, and now we're looking at Established A, Established B and Novel methods.

Added clarifications are provided for FDA's review policy for new sterilization technology: validation data and accountability. That's the underlying theme, the key message that we're looking for, that we mentioned earlier.

So we want to know one way or another, whether the validation data is sufficient because it is in conformity with existing standards or because we've looked at it already; or want to know that we haven't looked at it and now is the time for us to take a look at the new validation data.

Pyrogenicity recommendations and information requested have been updated, and updated guidance and expanded references have been provided throughout the guidance document.

So that takes us to the end of the presentation period. We're going to open it up for questions. If for some reason you don't have a chance to get your question in or formulated today, we recommend that you get in touch with the Division of Industry and Consumer Education.

You can just Google fda.dice. I'm sorry FDA and DICE and it'll be the first thing that pops up, or you can just use this connect right here: DICE@fda.hhs.gov.

Thank you very much and at this point in time I think we'll open it up for questions.

Coordinator: And with that if you do have a question at this time please press Star 1 and record your first and last name at the prompt.

Your name is required to introduce your question in the conference. Again that is Star 1 if you do have a question at this time. It will take just a moment for questions to come in. Please stand by.

Our first question will come from Mary Dadone. Your line is now open.

Mary Dadone: Thank you very much. This is Mary Dadone from Noxilizer. We're a new sterilization technology, nitrogen dioxide.

We understand that we are currently classified as novel. We are of course in discussion with the FDA.

Our understanding is that this guidance provides a migration path from the novel category to the established Category B. Could you comment on that?

Steven Turtill: Sure. I'm glad you mentioned that because that's an item that was actually related to the very last - the previous slide.

And that is a question that's come up as recent - as long ago as the 2002 version, and the 2008 draft. Is this a static classification system or is it dynamic and is it possible that methods can move from, for example, from Novel to Established B or from Established B to Established A?

And the answer is that it's not static. It's a dynamic system. And with more experience that we gain, and with more knowledge that we have of these systems and the confidence that we have of these systems, that it's very possible that a method can move from one of the categories to another one.

Mary Dadone: Thank you.

Coordinator: Our next question will come from (Emily) of 3M. Your line is open.

(Emily): Regarding the pyrogenicity claim updates they've added in implants but it doesn't classify what type of implants.

Our dental implants since they do not contact blood, circulating blood, are they included in this new blanket or are they still excluded from pyrogenicity requirements?

Steven Turtil: Well the language and the guidance is similar to the language that's in the USP and it's also in ST72.

If you have questions about your particular device type we encourage you to get in contact with the division that reviews that particular device type because the guidance's are general. They're not always all-inclusive.

It's quite often that, for particular device type, for neurology or for ophthalmic devices or in this case dental devices, they may have additional recommendations or things that they're looking for. So we strongly recommend that you get in contact with, in this case, the Dental branch.

(Emily): Okay thank you.

Coordinator: And our next question will come from Heather Nigro of NxStage Medical.
Your line is open.

Heather Nigro: Hi good afternoon. I was questioning whether or not the guidance indicates that the FDA will inspect the facility for those utilizing a novel sterilization technique.

And I'm wondering is this a mandatory inspection similar to a preapproval inspection for a PMA, or is it rather a goal of the FDA whereby you could actually obtain 510(k) clearance without an inspection taking place?

Steven Turtil: I think this may be a case by case situation. It depends on how much information comes in with the submission, how much information may already be known by the agency, and how much not.

It may be case by case but it does - the guidance does layout both options. And again, it may be very much case by case. I don't know if somebody else here may have a comment they'd like to add on that. Okay.

Coordinator: We'll take our next question.

Man: Hello? I have a question about - we have several products, you know, they are vascular device contact in blood. And but they are clear the (2000) K before this guidance document so they are not labeled as non-pyrogenic.

So is FDA implementation is for those product already cleared on the market to be non-pyrogenic and it's just for new 510(k) for the future submissions? So that's my question. If yes, how much time we have to be in compliance? That's my question.

Rebecca Nipper: Thank you. I think that we would - my name is Rebecca Nipper. I'm with the Office of Device Evaluations.

I think that we would expect that moving forward in your submissions you would provide that information but we are not expecting you to submit a new submission in order to provide that information on your existing devices.

Man: Okay. So does that mean for the product already cleared in the previous 510(k) we don't need to change the label to label it as a non-pyrogenic even if they are blood contacting?

Steven Turtill: I'm sorry. I'm sorry could you repeat that? Is the question that do you have to go and retroactively...

((Crosstalk))

Man: Yes, yes. For the product already cleared to this day and we already choose not to put non-pyrogenic symbol on the label.

Are we required by FDA to put the non-pyrogenic claim on the label and substantiate that with testing for each lot? And that's just my question for product already on the market.

Rebecca Nipper: So I think we expected to label your devices appropriately for the device type that they are, the specific guidance and it is not, so it is a recommendation.

But you should follow other regulations for proper labeling of your device to determine whether or not you should be labeling your device as non-pyrogenic.

Steven Turtil: And it's to your advantage to go ahead and take a look at the guidance within the standards that address this and carefully make a determination about what you want to do moving forward.

But you can also implement testing for devices that you currently have 510(k) clearance on. That's an option for you and it's probably to your advantage if you make that assessment and determine that it's a valuable thing to do.

Man: Okay. All right just to be clear that is basically that's not FDA's position to retrospectively require labeling of those - or if they're on the market just by this guidance document? We should follow whatever other document you said for that particular device for the assessment? Is that true?

Steven Turtil : Correct.

Man: Okay, thank you.

Coordinator: Our next question will come from (Pamela Barrows) of HCM. Your line is open.

(Pamela Barrows): Oh, good afternoon. My question is about pyrogenicity. The slide said that alternatives to batch release are acceptable but if you have a sampling saying in the justification.

And my question is would the FDA expect a risk assessment for (ST72) or when other formats for justification be acceptable? Thank you.

Steven Turtil: I think that really depends on what the justification is and how well it's substantiated.

So, you know, we would encourage you to get in contact with the branch and the division that would be reviewing that particular device type and discuss it with them.

(Pamela Barrows): Thank you.

Coordinator: Our next question comes from Dennis Guilfoyle of Johnson & Johnson. Your line is open.

Dennis Guilfoyle: Yes hi. Thank you very much for taking my question and a very nice presentation. I appreciate it.

One of the things that we often need to know are names of individuals within the FDA specifically the CDRH who are considered the experts in let's say, in the case I'm asking for is the endotoxin area.

If I was to want to talk to somebody with the expertise in endotoxins on medical devices who can I contact and who would that individual be?

Steven Turtill: I think the best way to get in contact with the experts, with any expert but that particular area, is to go through DICE. D-I-C-E that's still up on the screen there, the Division of Industry of Consumer Education.

They'll be able to connect you with, not only one of the experts for that, but also may be able to steer you toward somebody who knows something about your product line in particular.

Dennis Guilfoyle: Okay. Thank you.

Coordinator: And again if you do have a question at this time it is Star 1. Please do record your first and last name at the prompt.

Our next question will come from Stephen Inglese of Quality Solutions and Support. Your line is open.

Stephen Inglese: Yes ma'am. Good afternoon and thank you for taking my call. We support small business manufactures, device manufacturers in the industry for regulatory equality.

On the regulatory side with 510(k) in particular where pyrogenicity testing is required, would it be acceptable if the manufacturer of the material provides testing to us for that submission, versus the actual device itself that has that material contained within? Would that be acceptable sir?

Steven Turtill: Are you talking about for the pyrogenicity testing in particular?

Stephen Inglese: Yes sir, I am.

Steven Turtill: So there are a lot of tests in particular where we really want to see data based on the final finished product. And this is an example of that.

So we don't know how the materials are going to change or how the bioburden might change, or any other contaminants might change, from when the raw material is produced to when what is actually on the final finished product. So that's our recommendation there.

Stephen Inglese: Understood, thank you very much.

Coordinator: Our next question will come from Heather Nigro NxStage Medical. Your line is open.

Heather Nigro: Thank you. I have a question about filtration methods. I noticed that the guidance is the filtration methods and aseptic processing are outside of the scope. Does that mean that FDA won't consider any new filtration methods as novel?

Elaine Mayhall: This is Elaine Mayhall, reviewer at the Infection Control Devices Branch.

This guidance is focused on sterilization and microbial kill and not the exclusion of microbes. So it wouldn't be considered as a novel method. It would be covered by other guidances and the tenants of the aseptic process.

Heather Nigro: Okay. Yes thank you.

Coordinator: Our next question will come from Tessie Smith of Abbott Medical Optics. Your line is open.

Tessie Smith: Hi. I know that we set for the guidance that an established category is sterilization method, we do not need to submit any data like say the half cycle method.

I was wondering if there is any specific information that the FDA would like to see in our submission regarding these methods if we are not submitting the data itself?

Steven Turtill: For if you're not submitting what itself?

Tessie Smith: The data.

Steven Turtill: Oh.

Tessie Smith: The guidance talks about how we do not need to submit the data so I was wondering for an established category a sterilization method if there's any specific information that FDA would like to see included in the body of the submission if the data is not being provided like say the half cycle method or other methods a sterilization?

Steven Turtill: Right. If you go through the guidance document and take a look at the particular things that are asked for in each category, that should be able to help you out a lot.

So we're not looking for a tremendous amount of information regarding the validation in particular. Again we're very comfortable with including identification of the method that is used to validate, so you will want to spell out half cycle method if that's what you used, or some other method.

But we're not looking at that [validation data] for Established A in detail. We're very comfortable with the idea of you being in conformance with an FDA recognized standard.

And that's not to say that it all doesn't have to be conducted and documented and on file at your facilities, because the Office of Compliance is really responsible when they do their inspections, for taking a look at that.

So all of it has to be done, but for the obtaining of a 510(k) clearance, we're looking for the information that is actually outlined in this guidance document.

Tessie Smith: All right thank you.

Coordinator: Our next question will come from (Stacy Bennell). Your line is open.

(Nicholas Sintolacus): Hello. This is actually (Nicholas Sintolacus) instead of (Stacy).

But the question is has there been any consideration for the information required in the 510(k) submission where that submission's only purpose is to support a design change on the product where there's no change in the sterilization method? That's the whole question.

Rebecca Nipper: Sorry. This is Rebecca Nipper, ODE. So you're saying that you've made a design change. You have not changed the sterilization method at all?

(Nicholas Sintolacus): Yes that's correct.

Rebecca Nipper: So I think you would follow the normal procedures just like you would any other time that you make a design change to your device.

So if you under say are a special 510(k) program if you previously would not have needed this in the sterilization information you still wouldn't. I don't think this guidance changes that.

Steven Turtill: Right. I agree. I don't think this guidance changes it. And if you're looking for more information on that in particular, there is an FDA guidance document which is entitled pretty close to: Deciding when to Submit a New 510(k) Document. And there's a section in there that does address changes in sterility.

And two of the highlighted items in there are; one is if the SAL has changed, the Sterility Assurance Level, and the other one is if the change in sterilization method affects the performance of the device.

(Nicholas Sintolacus): Yes.

Steven Turtil: But I would encourage you to take a closer look at that.

(Nicholas Sintolacus): Sure. I guess I was asking more with respect to pyrogenicity testing and pyrogens, the information that would need to be included with regard to pyrogines for the same sterilization method?

Steven Turtil: Okay. So if there is a design change and perhaps you're using different materials or more materials or anything that could really affect the pyrogen levels, the bacterial endotoxin levels on the device, we would expect that you have in place, your routine conduction of pyrogen testing would account for that.

(Nicholas Sintolacus): Okay. So basically you're saying that it's a design change could impact pyrogen, pyrogen levels on the device then we should show that appropriately?

Steven Turtil: I would test that right up front.

(Nicholas Sintolacus): Yes.

Steven Turtil: I would encourage testing that right up front and become - it would be an integral part of future ongoing lot release testing of the product.

(Nicholas Sintolacus): Absolutely, okay. Thank you. That helps.

Steven Turtill: Okay.

Coordinator: Again if you do have a question that is Star 1 at this time. Our next question in the queue will come from (Terry Juan) of (NeoMedix). Your line is open.

(Terry Juan): Hello hi. This is (Terry Juan) from (NeoMedix). I have a question regarding to package test data.

So according to the guidance actually from it seems like both from 2016 and 2008 the package test data is not required for submission.

So is it possible you can provide some guidance on how then we should provide shelf life data? So for example we plan on doing for five years shelf life to accelerate rate of aging and real aging studies.

However we'll obviously submit our 510(k) way before that's complete. At which point can we submit our package to the agency? Can we submit as soon as our methods are solidified rather than the study complete? That's my question. Thank you.

Steven Turtill: Okay. I think there are actually a couple points there that are relevant. Going back to the K90-1, the 1990 version, we're looking for a description of the packaging, but not the package data itself.

But ever since then, and through now, what we're looking for - it is incumbent upon the Office of Compliance to be able to take a look at that data which should be on file with your office for any of the products for which you have received 510(k) clearance.

Another, a better way of saying that is while we may not look at it when a 510(k) is submitted it - all of the validation testing for all of the processes should be conducted and all the data on file with the applicant.

When it comes to package integrity shelf life testing, again some divisions don't particularly look at expiration date and shelf life claims on the package during the 510(k) process.

If you make a claim you should have the data on file. And for some device types in particular, depending on the division that they are reviewed by, they do want to see expiration validation dating, data. So it should be included in that submission.

And I think a little bit more to the point of your question, we do accept for 510(k) submissions, we do accept accelerated aging as a simulation.

Obviously if you want to put a five year shelf life claim on a product, to do real-time dating, real-time validation of that would take you at least five years.

So we accepted for a long time, the premise that accelerated aging is an adequate approach for simulating aging and following it with a good seal strength test would give you sufficient data to support your shelf life claim. Does that answer your question?

(Terry Juan): It does. Thank you.

Steven Turtill: Okay. And obviously accelerated aging can be performed in a much shorter time period.

Coordinator: And at this time I'm showing no other questions in the queue. If you do have a question please press Star 1 at this time and record your first and last name at the prompts.

Again that is Star 1 if you do have a question at this time. It'll take just a moment for questions to queue.

Our first question will come from (Marsha Palmer) of (NIMSA). Your line is open.

(Marsha Palmer): Hi. I just had a question about the, previous question about their accelerated aging. Because we have found that accelerated aging is not always accepted for the shelf life and that FDA has required real-time data before it gives us a shelf life of, you know, past six months.

Steven Turtil: Well for the purposes of clarifying the question we're basically talking about sterility issues here and package integrity for that whatever claim is on there. But there may be other issues that come up.

So with regard to the product performance or components of the device...

(Marsha Palmer): Okay.

Steven Turtil: ...performance of the product is a separate shelf life issue. Is that - are you asking just about the packaging and shelf and...

(Marsha Palmer): Well it's...

Steven Turtil: ...the maintenance of sterility?

(Marsha Palmer): Well it's when your final - yes your final device it's a little hard to separate the two. You know, you can't release your packaging without releasing the whole device so it really doesn't get you anywhere.

You know, if you can use the five year accelerated aging to release your package but you can't use it to release your product then it really doesn't benefit you.

Becky Nipper: This is Becky Nipper with ODE. I think if you are having or seeing inconsistencies in review processes I think the best thing you could do would be to notify us through other means. And we can try to resolve the issue internally if we're having inconsistency in particular areas.

(Marsha Palmer): Okay. And who would that contact be?

Becky Nipper: I think you could go through DICE, the information...

(Marsha Palmer): Okay.

Becky Nipper: ...that is up there and that will reach the appropriate individuals.

Marsha Palmer: Okay. Thank you.

Steven Turtill: Again there may be reasons - there may be a reason for that. Packaging should be reviewed consistently. But if there are certain coatings on devices, the reviewers from those particular divisions reviewing those particular devices may have good reason to say that we can't accept accelerated aging on this. That, progress of aging on this [the coating] may not follow first-order kinetics and we really want to see real-time aging.

Marsha Palmer: Okay.

Coordinator: Our next question comes from (Liza Riskoff) CooperVision. Your line is open.

(Olivia Ristal): Thanks. It's (Olivia Ristal). But this is (unintelligible) so my question is about what has been minimal - minimum shelf life data or the time of period or shelf life to be except in 510(k)?

For example if I have shelf life data is it within to six months of real-time or it's a six-month of real-time data?

Steven Turtil: I think I understand your question. I'll try to answer it. I missed - please feel free to repeat the question.

But for 510(k) submissions we look - we're willing to accept accelerated aging data but we accept that basically as a surrogate for real-time data.

So we expect confirmatory real-time testing to be done. So and...

((Crosstalk))

Steven Turtil: ...that's not a condition - submitting that data is not a condition of 510(k) clearance. Accelerated aging may be but the real-time data we expect just to be included in the file later on when it's completed.

(Olivia Ristal): Yes. Thank you I understand that. So - but at the time of the (unintelligible) what is the minimum period of shelf life? Because I read in there I think I read

the guidance is 14 a summation it was in there six months minimum so is it the - yes?

Steven Turtil: This guidance does not provide a specification for that. It depends on the device type again and it is also partly your call.

If you're trying to get a five year shelf life on something or a two year shelf life on something that's up to you to justify with your validation.

(Olivia Ristal): Yes. And I understand the states they how to say expiration date on the labels but, you know, so there is no (specific) requirements. Okay thank you very much. Thank you.

Coordinator: Our next question will come from John Schaefer CFI Medical. Your line is open.

John Schaefer: There is a long-standing guidance on bundling of multiple devices for a single submission and that guidance addresses conditions and means of determining what's a legitimate bundle?

Are the various elements of the new sterilization submission guidance consistent with that bundling approach?

Steven Turtil : I believe so if I understand your question correctly. There is a guidance related to bundling but there's also kind of looking at this in two different levels.

One is the guidance that addresses that specifically. Another one is sort of this issue of adopting products into existing validated families of devices.

For example for ethylene oxide sterilization, TIR 28 includes information as to how to make the assessment that for process adoption assuring that one product can be adopted into a family of devices that have already been validated based on a worst case configure - a worst case device.

So not seeing how this guidance really affects either one of those guidance's at all. All of the principles would still apply.

John Schaefer: Okay that's fine. I was only asking about the 510(k) side. We certainly understand the sterilization challenge family adoption side as a separate issue.

We have several thousand products. And a number of them can be reasonably grouped into large families that have common materials and common processes but differing geometries.

So all that I was talking about was the 510(k) side in relation to commonality of sterilization details so okay, thank you very much.

Coordinator: Our final question in queue will come from (Jared Shrozas) of Millstone Medical Outsourcing. Your line is open.

(Bill Zigma): Hi. My name - I'm actually (Bill Zigma) from Millstone Medical.

But we just had a question in regards to the pyrogen testing. What does the FDA consider a batch? Is it one single lot of product or can it be a whole batch of product which is sterilized at the same time? So we were just wondering if you could explain that a little bit?

Steven Turtill: That's a good question. I would really encourage you to take a look at ST72 for that. If that doesn't give you the answer because that has, that does provide

information in the body of the standard, as well as information in the annex it's about small batch release. So I would encourage you to refer to that.

And if it's not clear, we would encourage you to get in touch with DICE and find one of our experts to talk to about that. It's always good to have that information before rather than after making your submission.

(Bill Zigma): Okay thank you.

Coordinator: And with that I will turn the call back over to Miss Aihie.

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 Web page at www.fda.gov/training/cdrhlearn by Friday, February 19.

If you have any additional questions about the final guidance document please use the contact information provided at the end of the slide presentation.

As always we appreciate your feedback. Again thank you for participating and this concludes today's Webinar.

END