

NWX-HHS FDA

Moderator: Irene Aihie
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Coordinator: Good afternoon. Welcome to today's conference call. At this time, all lines are on listen only for today's conference until the question and answer portion of our call, at which time you will be prompted to press star 1 on your touchtone phone.

Please ensure that your line is unmute and please record your name when prompted so that I may introduce you to ask your question. Our conference is being recorded, and if you have any objections you may disconnect at this time. I will now turn the conference over to your host, Ms. Irene Aihie. Ma'am, you may proceed.

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 March 12, FDA published the final guidance document titled, "Reprocessing Medical Devices in Healthcare Settings: Validation Methods and Labeling."

The focus of today's webinar is to help manufacturers understand the recommendations described in this final guidance document and provide further clarification where necessary. Your presenters are (Geetha Jayan), a

Senior Science Health Advisor from the Office of the Center Director, and (Elaine Mayhall), a Scientific Reviewer from the Office of Device Evaluation.

Following the presentation, we will open the lines for your questions related to topics in the guidance only. Please note that questions about specific products should be directed to the appropriate review office. Other Center subject matter experts are also available to assist in the question and answer portion of our webinar.

Now I give you (Etha).

(Geetha Jayan): Thank you, Irene, and good afternoon everyone. I'm (Geetha Jayan), a Senior Science Health Advisor in the Office of the Center Director at CDRH. As Irene mentioned, the purpose of this webinar is to go over the major topics in FDA's final guidance on "Reprocessing Medical Devices in Healthcare Settings: Validation Methods and Labeling."

At the end of the presentation, we will also clarify manufacturers' questions on information provided in the guidance document. The draft of this guidance was published and opened for public comment in 2011. We received 487 public comments on the draft. The comments came from various stakeholders, including device manufacturers, test labs, trade and professional organizations, and users.

A common theme in the public comments was the request to provide additional information and clarification on various concepts and sections in the document. For example, there were requests to better clarify the scope of the document, specific criteria for reprocessing instructions, and few other sections.

There were also comments requesting that FDA provide more information on resources and references for developing reprocessing instructions. All comments were carefully considered as the guidance document was finalized and published last week.

This is an outline of today's presentation. So the focus is the final guidance document titled, "Reprocessing Medical Devices in Healthcare Settings: Validation Methods and Labeling." First, we will take a look at the purpose of the guidance document and the scope of devices covered.

Then we will go over the major topic areas covered in the document. This includes an overview of reprocessing, FDA's six criteria for developing reprocessing instructions, and recommendations for validating the cleaning process. And finally, we will go over the summary of key messages from the guidance document before we move on to the question and answer session.

So what is the purpose of this guidance? As you know, devices that can be reused are commonplace in healthcare settings. To reduce the risk of patient infections during reuse of these devices, it is important to reprocess them properly between uses. And a device manufacturer's reprocessing instructions are critical to ensure their proper reprocessing.

This guidance document provides recommendations to medical device manufacturers for developing reprocessing instructions that can be easily understood as well as followed by users. This is to help ensure that reusable devices remain safe and effective for use on patients after reprocessing.

This guidance document also outlines the Agency's current recommendations to manufacturers on how to conduct scientifically sound testing to validate the reprocessing methods and instructions.

In addition, this guidance also describes new measures the Agency is taking to enhance its oversight of the reprocessing of reusable devices. For example, in Appendix E of the guidance, FDA has identified a subset of medical devices that pose a greater likelihood of microbial transmission and represent a high risk of infection if they are not adequately reprocessed.

So the 510(k) submissions for these devices in Appendix E should include protocols and complete test reports of the validation of the reprocessing instructions. And finally, this final guidance document replaces FDA's 1996 guidance document titled, "Labeling Reusable Medical Devices for Reprocessing in Healthcare Facilities."

So let us take a look at what is new in this guidance document when compared to the 1996 guidance document it replaces. So reprocessing, as you know, is a complex process that starts with cleaning, followed by sterilization or disinfection. And the entire process needs to be validated to ensure it works properly.

Recommendations in this 2015 guidance document have been expanded to include information applicable to validation of the reprocessing methods and instructions. For example, specific emphasis is given to the importance of proper cleaning to ensure that the device is adequately prepared for the subsequent sterilization or disinfection steps.

Recommendations are also provided for proper validation of the cleaning method, as well as instructions for cleaning. This document also emphasizes the importance of device design that is less challenging to reprocess. And it also provides recommendations on human factors that are important when validating reprocessing methods and instructions.

Another new aspect in this guidance is that it provides greater clarity on what documentation needs to be provided in the different types of premarket submission that fall under a PMA, HDE, de novo, an IDE or an HDE.

So next let us look at the device type for which the recommendations in this guidance document are applicable. The recommendations in this guidance are applicable to four types of devices. First, reusable devices that are supplied as sterile to the user and requires the user to reprocess after each patient use.

Second, reusable devices that are supplied nonsterile to the user and requires the user to process prior to the initial use of the device, as well as reprocess after each use. Third, reusable devices that are intended for use by a single patient and are to be reprocessed between each use. And fourth, single use devices that are supplied as nonsterile to the user and requires the user to process prior to its use.

Now I turn it over to Dr. Elaine Mayhall, who will walk you through the major topic areas covered in the guidance starting with an overview of the various steps involved in reprocessing.

(Elaine Mayhall): Thank you, Geetha. Good afternoon. This is Elaine Mayhall. I'm a reviewer in the Infection Control Devices Branch in ODE. This diagram is an overview of reprocessing from the point of use processing step to cleaning and finally disinfection or sterilization.

Cleaning, disinfection, and sterilization are distinctly different processes and should be validated separately and independently. Point of use processing is the initial cleaning steps that are intended to prevent drying of soils on the

device surfaces prior to cleaning. Cleaning is the physical removal of soil, and disinfection and sterilization are intended to kill microorganisms.

In recent number of years there has been an evolution towards the development of more complex devices with designs that are more difficult to reprocess. However, there has also been significant advances in knowledge and technology involved in reprocessing reusable medical devices. The recommendations in this guidance reflect the scientific advances in these areas.

The formulation of instructions for reprocessing a device starts in the early stages of device design and engineering. For example, device designs that pose a significant challenge to reprocessing include shaft-within-lumen configurations, fine channels, seals, and mated articulating surfaces.

Less challenging alternative designs include single-use parts, flush ports, and dedicated cleaning accessories. Manufacturers should consider using designs that facilitate cleaning, disinfection, and sterilization methods that are easily and effectively implemented by users.

Device labeling should provide instructions on how to prepare the device for the next patient use and should identify materials and equipment that will be needed and are readily available to users.

Also, in developing your reprocessing instructions, you should consider human factors, including the use of consistent reprocessing instructions for all devices of a type. Using consistent terminology and the same document layout will improve the user comprehension and adherence.

You should address any known post-market human factors issues that exist for reprocessing your device or similar devices. For example, actions requiring substantial dexterity, strength, good visual acuity, or familiarity with uncommon practices present human factors challenges.

As part of your design control, you should validate your reprocessing instructions to ensure that users will thoroughly understand and follow them. The guidance document includes recommendations for designing a human factors study of reprocessing instructions.

As in the 1996 guidance document, this new guidance document includes the criteria for clear reprocessing instructions that will ensure users understand and correctly follow the reprocessing instructions. The list of criteria has been condensed from seven criteria to six criteria.

The reprocessing instructions should reflect the intended use of the device, should advise users to thoroughly clean the device, should indicate the appropriate microbicidal process for the device, should be technically feasible and include only devices and accessories that are legally marketed. Finally, the instructions should be comprehensive and should be understandable.

Criterion 1: The reprocessing instructions should reflect the intended use of the device. The appropriate reprocessing instructions depend on the physical design of the device, the intended use of the device, and whether it has direct or indirect contact with the patient. They also depend on the type and extent of soiling and contamination the device is exposed to during clinical use.

In addition, it depends on the use of disinfectants or other chemicals that might leave harmful residues or adversely affect device materials or

performance if inadequately rinsed, and any specific or unique risk to the patient or the user.

Criterion 2: Reprocessing instructions for reusable devices should advise users to thoroughly clean the device. Cleaning is the first step in reprocessing. Adequate sterilization or disinfection depends on the thoroughness of cleaning. If it cannot be cleaned, it cannot be disinfected or sterilized.

Details of the cleaning procedure will vary depending on the complexity of the device and may include disassembly of the device, use of protective covers to reduce soiling, and flushing of the device internal structures.

Criterion 3: Reprocessing instructions should indicate the appropriate microbicidal process for the device. Your instructions should be consistent with current infection control principles. The microbicidal process recommended is dependent upon the intended use of the device and is described by the Spaulding Classification for critical, semi-critical, and noncritical medical devices.

Critical devices are introduced directly into the bloodstream or contact a normally sterile tissue or body space during use. Examples of critical devices include surgical instruments, irrigation systems for sterile instruments and sterile tissues, endoscopes used in sterile body cavities, such as laparoscopes, arthroscopes, and intravascular endoscopes, and all endoscope biopsy accessories.

Microbial transmission from critical devices and the risk of infection if the device is not sterile are likely. These devices should be disassembled, if possible, and thoroughly cleaned and sterilized after each use.

Semi-critical devices contact intact mucous membranes or non-intact skin, but do not ordinarily penetrate tissues or otherwise enter normally sterile areas of the body. Examples of semi-critical devices include endotracheal tubes, bronchoscopes, laryngoscope blades and other respiratory equipment, esophageal manometry probes, diaphragm fitting rings, and gastrointestinal endoscopes, such as duodenoscopes.

These devices should be thoroughly cleaned and then sterilized. Intact mucosal surfaces are relatively resistant to small numbers of spores. Therefore, if sterilization is not feasible then semi-critical devices should be high level disinfected following thorough cleaning.

Noncritical devices contact only intact skin and do not penetrate it. Examples of noncritical devices include blood pressure cuffs, stethoscopes, and skin electrodes. Also, devices that do not directly contact the patient but may become contaminated with microorganisms and organic soil, including blood or body fluids, during patient care are considered to be noncritical devices.

Examples of these types of devices include infusion pumps and ventilators. These devices may not be visibly contaminated. However, they should be thoroughly cleaned and then receive intermediate or low-level disinfection, depending on the nature and extent of the contamination.

Noncritical devices that may be contaminated with blood or body fluids that may contain blood-borne pathogens should be cleaned and then receive intermediate-level disinfection with a product that has an EPA registered claim for activity against Hepatitis B.

Criterion 4: Reprocessing instructions should be technically feasible and include only devices and accessories that are legally marketed. Reprocessing

instructions should be technically feasible in the intended location, such as in the home or in the healthcare setting. The equipment and accessories needed to implement the instructions should be available for users to obtain.

For example, the type and size of the brush required to clean a device lumen should be readily available. Also, the type of sterilizer with manufacturer-validated sterilization cycle parameters and accessories should be available to the users.

For example, sterilization instructions should not recommend radiation sterilization for reusable devices because radiation sterilization generally is only used in manufacturing facilities.

Steam sterilization is the most common method of sterilization used in health care facilities. Ethylene oxide, hydrogen peroxide, ozone and liquid chemical sterilization processes are also available in some health care facilities.

Sterilization methods and parameters should be technically feasible. Extended cycles is an example of cycles that are not technically feasible. The specifications for these cycles deviate from those found in commonly used FDA-cleared sterilizers and have limited or no FDA-cleared sterilization accessories.

They typically include longer exposure times and/or higher or intermediate temperatures. These limitations can pose serious technical challenges in healthcare facilities.

Criterion 5: Reprocessing instructions should be comprehensive.

Comprehensive instructions enable the user to understand precisely how to implement the entire reprocessing procedure safely and effectively.

The instructions should include all of the following elements. Special accessories and any special protection during reprocessing, such as valves, plugs, or stoppers to prevent ingress of harsh chemicals or water, special tools, sizes and types of brushes, flush port connectors, and connector size specifications.

Point of use processing or pre-cleaning instructions should be included. The instructions should include disassembly and reassembly instructions, including step-by-step instructions with visual aids and should indicate whether the device should be reassembled before or after sterilization.

The method of cleaning: The instructions should include a detailed validated method for cleaning. The information should provide a list of parameters including duration of each processing step, temperatures, and water quality.

You should list the cleaning agent or the class of cleaning agent used in your validation testing. The labeling should include information on its preparation and use or refer the user to the manufacturer's instructions.

You should include instructions for rinsing the device following cleaning to remove processing chemical residues. The instructions should identify the type and quality of water that should be used and the duration, volume, and temperature of the water.

You should identify a lubricating agent, if required. Validation of reprocessing methods, including disinfection and sterilization, should include the lubricating agent. After cleaning, the labeling should instruct the user to visually inspect the device for cleanliness, and if the device is not visually

clean, the instructions should advise the user to repeat the cleaning process or to dispose of the device.

The labeling should include instructions for drying the device after processing and before storage. You should identify the method of disinfection or sterilization, including the validated cycle parameters and the accessories that should be used. You should provide information on specifications of the device design to be sterilized and the packaging and load characteristics.

Labeling should include instructions for reducing sterilant residuals following sterilization by ethylene oxide, hydrogen peroxide, or other processes that may leave sterilant residuals on the device. For example, rinsing is used for liquid chemical sterilants and aeration for ethylene oxide.

Instructions should include drying the device. Devices should be thoroughly dried after processing and before storage. The labeling should either inform the user how many times the device can be reused based on testing or provide the user with a mechanism or method to ascertain whether the device has exceeded its use life, including a method to establish that the device is still within performance specifications.

Label instructions should include additional recommendations, such as for devices that are initially supplied non-sterile to the user and require the user to sterilize the device before use. These devices should be labeled non-sterile directly on the individual device packaging to ensure a non-sterile product is sterilized before use.

For a device intended to be maintained by a patient or lay care provider, the labeling should include reprocessing instructions that are understandable to a lay person and can be performed at home. Labeling may also refer the user to

guidelines from professional organizations or OSHA. And of course, the instructions should include the manufacturer's contact information.

Criterion 6: Reprocessing instructions should be understandable. The instructions should be clear and legible. The instructions should be presented in a logical, sequential order from the initial processing step through the terminal processing step, and should be described using as simple language as possible.

The instructions should be sufficiently detailed to explain the correct procedures for all steps. The use of charts, diagrams, and pictures that can be posted in a work station are helpful in ensuring adherence to reprocessing instructions.

Now we turn to reprocessing validation and the cleaning process. You should conduct validation activities to demonstrate that your methods are adequate to allow the device to undergo further processing to eventually be reused safely, and that your reprocessing instructions are effective in conveying the proper reprocessing method to the user.

This section is significantly different from the 1996 guidance document and provides information on the methodology recommended for cleaning validation studies. Your validation testing should include the worst-case implementation of the cleaning process, use soils that are relevant to the clinical use conditions of the device, and should include predetermined cleaning test end points.

The artificial test soil should represent materials that the device would likely be exposed to during actual clinical use and would create the greatest challenge to cleaning. For example, during visualization of the larynx, a

laryngoscope would likely be exposed to both blood and mucous. The artificial test soil should be a multi-component soil that includes substances that simulate both blood and mucous.

The application of the test soil should mimic worst-case clinical conditions and the device should be inoculated in all locations likely to contact patient material, especially all locations that are difficult to clean, such as mated surfaces, lumens, and hinges.

The test devices should be exposed to simulated use conditions that incorporate multiple full use cycles, assess the accumulation of soil over time, and account for real-world use conditions and mimic worst-case clinical use. For example, you should conduct all functional procedures, such as repeated articulation, flexures, and manipulations, in order to soil the device sufficiently.

Powered hand-pieces and electrosurgical instruments should be powered on, to simulate use conditions. The validation protocols should use, for example, the shortest time, lowest temperatures, and weakest solution for each step of the cleaning instructions. For example, if the instructions recommend a 10-20 minute pre-soak, the validation protocol would specify 10 minutes as the soak time.

A side-by-side comparison of the label cleaning instructions and the cleaning process used in the validation protocol should be prepared and provided. FDA recommends that you use at least two quantitative test methods capable of directly measuring clinically meaningful levels of a test soil to meet a relevant predetermined cleaning end point.

For example, protein, total organic carbon, and hemoglobin assays. You should validate the quantitative test methods you choose to measure residual soil, including for analytical sensitivity and specificity.

Exhaustive extraction and extraction using a known quantity of soil are commonly used extraction methods. Recovery efficiency should be determined as part of the validation of the extraction method. All surfaces should be sampled, including internal surfaces and mated surfaces.

You should use an appropriate extraction volume to remove the test soil from the device. For example, if the volume is too large the test marker will be diluted below the level of detection for the assay.

Testing should include appropriate controls, including a negative device control, which is unsoiled but undergoes the same cleaning and extraction process as the test device; a positive device control, which is soiled with a known amount of soil, but is not cleaned and residual soil is extracted; a negative sample control, which is an extraction with no device and serves as a blank; and a positive sample control, which is an extraction with a known amount of soil but with no device.

This last control serves to address interference of the extraction fluid and extraction method with the soil detection.

The microbicidal processes should be validated. For example, with disinfection you should demonstrate that the device can be disinfected to the appropriate disinfection end point using contact conditions that are consistent with those specified in labeling for the legally marketed disinfectant and under worst-case conditions.

For sterilization, FDA recommends validation of cycle specifications that are consistent with the conventional parameters as listed in Appendix C of the guidance document. For pre-market review, FDA will review the reprocessing instructions included in the labeling when we review pre-market submissions for reusable medical devices.

All cleaning, disinfection, and sterilization procedures should be validated and validations should be completed prior to submission of your pre-market application. For PMAs, HDEs, and de novos, protocols and complete test reports of validation of reprocessing instructions should be submitted.

For 510(k)s, FDA expects manufacturers of a subset of devices listed in Appendix E to include data in 510(k) submissions to validate their reprocessing instructions. Validation data may be also requested as needed for substantial equivalence for other devices. For IDEs, a summary of the validation reprocessing instructions and methodology should be provided.

The key messages of the guidance document are that manufacturers should provide adequate labeling that includes instructions for reprocessing and reusing devices and device accessories safely. All cleaning, disinfection, and sterilization procedures provided in the labeling should be validated.

Finally, the labeling should provide sufficient instructions on how to prepare the device for the next patient use. Manufacturers should identify the materials and equipment that the users will need to reprocess the devices, and these materials and equipment should be readily available to users.

That concludes my formal presentation and now we will take questions from the audience.

Coordinator: Thank you. At this time if you wish to ask a question, please press star 1 on your touchtone phone. Once again, if you would like to ask a question, please press star 1. Please ensure that your line is unmuted and please record your name to be introduced for your question.

Please stand by for our first question. Our first question is from (Pentose Medical). Your line is open.

Woman: Great. Thank you. We really appreciate FDA's guidance regarding reprocessing. This is obviously a challenge for a lot of companies, and we appreciate the opportunity to talk directly to you about the guidance document.

One thing that FDA noted in the guidance was that all relevant internal surface areas should be sampled during the extraction method, and in some cases additional disassembly processes may be required to adequately extract residual soil.

So what we're wondering is if FDA could describe this expectation specifically regarding side-viewing duodenoscopes and whether or not the expectation is different for these scopes compared to other endoscopes.

(Geetha Jayan): Thank you for your questions. So the expectation is applicable to all reusable devices. I mean, it's not applicable to any specific category. The recommendations in this guidance are applicable across the board to all reusable devices in general.

Woman: Okay. Great. And with regard to the requirement for the potential for disassembly of the devices during cleaning, can you speak a little bit about that and when that might be required?

(Elaine Mayhall): This is Elaine Mayhall. I think in general we wouldn't expect you to do disassembly beyond the normal disassembly that the user would be doing for the device. So we wouldn't expect destructive testing unless - there may be a situation where you have to demonstrate that liquids are not getting through or past those mated surfaces and into other areas. But in general we wouldn't expect to see - expect you to do destructive testing.

Woman: So in the example you just provided, are you talking about liquid seeping beyond, for example, O-rings?

(Elaine Mayhall): Right.

Woman: So in that case, would you expect that we disassemble the scope to the point of the o-rings? Because that's not something that the user would typically do.

(Elaine Mayhall): I think there are some special situations, and I think that's really beyond the scope of this discussion right now. So you can always address that to the review office for the device.

Woman: Okay. Thank you.

(Elaine Mayhall): You're welcome.

Irene Aihie: Operator, we'll take the next question.

Coordinator: Next question is from (Sanjay Urick). Your line is open.

(Sanjay Urick): Hi. Thanks for the good presentation. In Section 5, it specifies that manufacturers provide their contact information. Now does the contact

information have to be domestic? Our parent company is in Denmark, Copenhagen, and the instruction for use has their address. So it is mandatory that we use a U.S. address on the IFU, or the instructions for use?

(Geetha Jayan): Could you please repeat the question?

(Sanjay Urick): Sure. In Section 5, it specifies that manufacturers should provide the contact information. The contact information has to be domestic or has to be U.S.? The contact information has to be the U.S. address or the U.S. phone number?

(Elaine Mayhall): Correct. It should be U.S. - the contact information for the manufacturer?

(Sanjay Urick): Yes.

(Elaine Mayhall): Okay. I don't think it has to be a U.S. contact, as long as the user can contact the company overseas. That would be fine.

(Sanjay Urick): Okay. Thank you.

Coordinator: Our next question's from (Teri McMann). Your line is open.

(Teri McMann): Hello there. I work with a contact lens manufacturer, and I've got actually two questions to ask. And the first one would be a contact lens, a gas permeable contact lens, would have some exposure to mucous, but have you actually categorized it as semi-critical or the non-critical? Do you know?

(Geetha Jayan): Thank you for your question. However, it appears to be a device-specific question. So we recommend that you submit your question to the DICE. The contact information is provided on the slide that is up there.

(Teri McMann): Okay. Tell me again who I'm supposed to contact. Sorry?

(Geetha Jayan): It is the Division of Industry and Consumer Education and the mail is D, as in David, I, C as in cat, E as in Edward, at F-D-A dot H-H-S dot G-O-V.

(Teri McMann): Very good. Thank you for that. It was helpful. And the second question is that you said that, you know that you had to indicate that the products you are using to clean and disinfect the product should say that it's a legally approved product. Now does that actually term need to be on the instructions for use or can you shorten it by saying like FDA approved or does that term itself need to be on there?

(Elaine Mayhall): You're talking about a disinfectant used on the contact?

(Teri McMann): You said during the webinar that you had to indicate that the product that you're using to clean, sterilize, disinfect, and needed to be legally approved. And I'm wondering if that's an exact term that needs to be on the instructions for use.

(Elaine Mayhall): Now the disinfectants are - the high-level disinfectants liquid chemical sterilants are FDA cleared. The low-level and intermediate-level disinfectants are Class I devices and need to be legally marketed per FDA, but they're also regulated by EPA. So they should be registered by EPA.

So you don't have to say in the labeling that they use a - to specify that the product is legally marketed. We'll look at that when we look at the review. But you should specify a type of disinfectant that is legally marketed.

(Teri McMann): Okay. So as long as we specify a brand or something along that line and it is approved, then we're good?

(Elaine Mayhall): Correct.

(Teri McMann): Okay. Very good. Thank you.

Coordinator: Our next question's from (Diane King). Your line is open.

(Diane King): Hi. Thank you very much. I have three questions. The first is from Criterion 5, the section that prefers to reduction of sterilant residuals. It refers specifically to EO and to hydrogen peroxide, and there's a reference to ISO 10993-7 for acceptable levels of EO residuals.

Do you consider that acceptable levels of hydrogen peroxide residuals have been established? And, if so, do you have a publication to which you refer to those?

(Steve Elliott): Hi. This is (Steve Elliott). Currently there are no established levels for hydrogen peroxide residuals. Concerns associated with hydrogen peroxide should be addressed through material compatibility of the device and biocompatibility.

So that would largely be device specific to provide that information. To my knowledge, that specific ISO standard doesn't contain any information along those lines.

(Diane King): Okay. Great. My next question involves whether the validations or the test results that the agency would expect to see in a 501(k) would cover the possible effects of combining or alternating between different validated sterilization methods over the life of the device?

(Steve Elliott): That is a complex question. I think that's something that might be needed to be addressed in more detail with the device-specific office, possibly through the pre-submission process.

(Diane King): Okay. All right. Great. Thank you. My last question pertains to Criterion 2, which mentions the use of protective covers and states that cleaning instructions should assume the worst-case situation in which the device is used uncovered.

I'm wondering whether the agency considers a scenario in which performance criteria for a device-specific protective cover could justify use of a critical device after disinfection rather than sterilization.

(Elaine Mayhall) I think that's more specific to the device. So it should be - you should talk to the device-specific office. But in general if a cover is used, whether it's considered to reduce the soiling and to make it easier to clean, so if it's supposed to be sterilized, it should still be sterilized.

There are a few exceptions to that, but they're specific devices with specific performance testing and so forth. So it would be best to talk to the device-specific office on that.

(Diane King): Okay. Great. Thank you.

(Steve Elliott): An additional comment with regard to the ethylene oxide residuals. The guidance document does refer to AAMI ST41 and, as you mentioned, ISO 10993-7. The most helpful information you'll find will probably in the ST41 for designing an aeration procedure.

(Diane King): Okay. Thank you.

Coordinator: Thank you. Our next question is from (Orte Tolla). Your line is open.

(Orte Tolla): Yes, hi. Thank you for the very good presentation. I have three questions for you. One is about the different clean agent. If you are recommending several cleaning agent, do you have to validate using each individual one or just the least effective?

(Geetha Jayan): Could you repeat the question once more, please? We were not able to hear you.

(Orte Tolla): Sorry about that. No, it's about if you are recommending several cleaning agent, do you have to validate each individual one, or is it enough to validate the one considered the least effective?

(Elaine Mayhall): Cleaning agents are a little bit difficult, because there are no standards for them and no regulation of them. So in general if you validate with a specific cleaning agent, you should reference that cleaning agent in your labeling or a similar class of cleaning agent, such as an enzymatic cleaner if you used that.

I don't know that you have to validate with every cleaning agent, but if you mentioned it in your labeling, you should probably do validation testing with each agent.

(Orte Tolla): Okay. Good. That's understandable. And the next...

(Steve Elliott): And one other thing in addition to that, if you have questions about which one's going to be the most or least effective, any validation design plan should really be put together such that you're testing worst case.

(Orte Tolla): Okay.

(Steve Elliott): So if you have an option in there, for example, the detergent says, the cleaning says, mix, for example, one ounce per gallon, you want to design your validation protocol so it's testing worst case. So you want to do one ounce per gallon at the most, but really to prove what's going on there, you'd be better off going a little below that.

(Orte Tolla): Okay. Good. Yes. Then the next one is about the number of cleaning cycles. Do you have any recommendation about how to select the number of cleaning cycle you want to use for your validation?

(Geetha Jayan): We don't provide any specific, you know, recommendations on specific number of cycles.

(Orte Tolla): Okay.

(Geetha Jayan): I mean, if this question is related to any specific device and in the scenario in which that is applicable, we recommend that you touch base with the appropriate review division.

(Orte Tolla): Okay. And I think it might be the same thing, how many samples would be most appropriate? We are talking here about non-critical devices.

(Geetha Jayan): Again, that would depend on what kind of device you're talking about. So, you know, that would be a question that you should reach out to the review division.

(Orte Tolla): Okay. Good. And that's enough. Okay. Thank you very much. That was very important information.

Coordinator: Thank you. Our next question's from (Robert Talmouth). Your line is open.

(Robert Talmouth): Thank you. Yes, this is about the cleaning procedure. I'm a molecular chemist, who has worked in the field of chemical detergency for many years, and I think it's well accepted that the cleaning chemistry for ultrasonic type cleaners have not been optimized for cleaning medical devices. They're typically generic enzymatic type cleaners that were designed for other cleaning applications.

And I was wondering if the FDA is going to make recommendations on specific cleaning chemistries that are better suited for removing biological debris?

(Geetha Jayan): We recommend that you select and validate whichever cleaning method is applicable to your device and provide that information in the device labeling.

(Robert Talmouth): Okay. The manufacturers of the ultrasonic cleaning equipment, I mean, handle that and the chemicals supplier doesn't often have a say in what type of cleaner is used. I mean, that's my only concern.

And it's, you know, it's clear to the organization that I represent that the cleaning chemistries could be optimized, could be improved. And it's a, you know, it's kind of well-accepted in the field that you could reduce and improve the cleaning cycle with different chemistries.

So that's the point I was making. I just wondered if the FDA, you know, would be making recommendations based on the cleaning chemistry or is that something that you wouldn't do?

(Geetha Jayan): Okay. So that is a specific question related to certain cleaning chemistries and technologies. And we recommend that you submit your questions to DICE, the Division of Industry and Consumer Education. Again, the contact information is on the slide that you see up there.

(Robert Talmouth): Okay. All right.

(Geetha Jayan): Thank you.

(Robert Talmouth): Okay. Thank you.

(Steve Elliott): And one additional comment on that. Its different cleaning chemistries are going to be more effective or less effective depending upon what they're supposed to be cleaning. So it depends on, as you'll see in the validation sections, there's emphasis on picking clinically relevant soils to simulate contamination and use.

And the cleaning chemistries that should be chosen should actually address what those contaminants are. So if something is going to be very high in protein or if something's going to be very high in carbohydrate, and you're choosing a different type of enzymatic cleaner, you want to choose the types that are lipases or proteases or whatever it is that you're looking for, so.

((Crosstalk))

(Steve Elliott): Go ahead.

(Robert Talmouth): Even perhaps if an enzymatic cleaner is not appropriate, that there are many, you know, cleaners based on ionic strength that work better, you know, without enzymes being present. So that is the whole point I'm making, that

there are lots of different chemistries out there. And I think probably they haven't been optimized for the removal of sort of biological debris.

I mean, as a chemist, you look at these sort of, you know, cleaning capabilities and you know that the cleaning process could be improved.

(Elaine Mayhall): Right. The cleaning process is important, and there are a lot of different methodologies that could be used. But it's really much more detailed than what we discussed in the guidance document. And it needs to be addressed in validation testing for the individual devices.

(Robert Talmouth): Okay. All right. That's good to know. Thank you.

Coordinator: Thank you. Our next question comes from (Michelle Alfa). Your line is open.

(Michelle Alfa): Thank you and just wanted to commend the group. It was a great presentation and helped clarify a lot of things. You mentioned under the cleaning validation section that worst-case conditions should be mimicked during the validation process. And you also indicated the use of two quantitative test methods.

And I was wondering if you could comment on devices such as flexible endoscopes that go into the colon and get exposed to microbes, in addition to organic material. If the enzymatic or the detergent that is being used in cleaning doesn't kill the vegetative bacteria, could your markers be, for instance, a protein quantitative marker and then a microbial viable level marker?

I do appreciate that the guidelines states very clearly spores aren't to be used, and that makes total sense. But since the purpose of the cleaning is also to

reduce the level of microorganisms present, I wondered if one of the markers could be viable microbe?

(Elaine Mayhall): Pretty much we recommend against using any kind of microbial log reduction for demonstrating cleaning, because we haven't seen adequate data that correlates the reduction of microbes on the device to removal of soil. So in general we're not going to - unless someone can provide data demonstrating that there is a correlation, we don't expect to see the use of microbial log reduction for cleaning validation.

(Michelle Alfa): Okay. The only reason I ask the question is the objective is really to make sure the microbe load is low enough so that when you do disinfection it will be expected to be effective. But I understand the comment that you made.

And the last question I had was I noticed that when you were talking about the Spaulding Classification, you have categorized bronchoscopes semi-critical. Could you expand on that a little bit, given that they do enter a sterile body space, in terms of going into the lungs?

(Elaine Mayhall): Well, in order to get to the lung, they have to go through the larynx and the throat, so you really should - and it contacts mucosa. So it's really a semi-critical device.

(Michelle Alfa): All right. I understand that, but I guess it's a bit confusing when, for instance, biopsy forceps that would go through an endoscope and may also go over the mucosal surface, the expectation is it should be a sterile device. But I appreciate your comment back on why it ended up in the semi-critical category.

(Elaine Mayhall): Right. Well, the use of the biopsy forceps may be a different situation in that case. But that would be a question really for the device review division.

(Michelle Alfa): Thank you.

Coordinator: Our next question is from Anita Kiprovska. Your line is open.

Anita Kiprovska: Thank you for your thorough presentation, FDA. We have two questions from Novus. The first one is does FDA have a position and preference for representative soils for fidelity to superbug cleaning sterility of validation?

(Geetha Jayan): Could you repeat your question one more time, please?

Anita Kiprovska: Certainly. Does FDA have a position and preference for representative soils for fidelity to superbug cleaning sterilization validation?

(Geetha Jayan): Okay. So as you can see in the guidance document, we do not, you know, we do not provide recommendations on what specific soil to select. We ask that, you know, whichever soil you select, it needs to mimic the conditions of use of the device, of the clinical use conditions of the device.

Anita Kiprovska: Thank you. The second part of the question is for positive device controls; does the new guidance address the soil accumulation over time and/or provide suggestions for methods on device-specific collection and simulation?

(Steve Elliott): Hi. This is (Steve Elliott). With soil accumulation, this is something that is expected to be addressed through validation testing. However, it is something that might vary from device to device.

So it could be a device-specific concern related to issues cleaning and processing a specific device line or device type within that. So probably that is a question that would need to be addressed by the device-specific office.

Anita Kiprovskaja: Okay. Thank you. And lastly, I had a question surrounding also the post human factors labeling. Can you expand a little bit more detail on that information?

(Geetha Jayan): Could you be more specific on, you know - I mean, we have a couple of paragraphs on the human factors, so what specifically are you looking for?

Anita Kiprovskaja: So what type of - when you say post human factors, that to me is implying the post-commitment marketing requirement that we have to monitor. Is that something that we have to execute post - I mean, after we get the device cleared?

(Geetha Jayan): So basically what we are saying is, you know, if you are aware of any issues, you know, any post-market issues that have occurred, those considerations need to be taken into account.

Anita Kiprovskaja: Okay.

(Geetha Jayan): And, you know, if you look at Page 7 of the guidance, we have provided a couple of examples there, you know, you should address your specific aspects such as, you know, actions that require substantial dexterity or strength, good visual acuity, familiarity with uncommon processes. So those are the kinds of things that need specific attention when you validate and provide your reprocessing instruction.

Anita Kiprovskaja: Okay. Thank you so much.

Coordinator: Our next question is from Shannon Scruggs. Your line is open.

Shannon Scruggs: Thank you. Good morning - or afternoon, I guess, at your time. I just wanted to be sure, because you may have said it at the beginning of the presentation, but we wanted to be really clear. Is the new guidance applicable only to new reprocessing devices, or is it applicable to all of our approved devices, even those approved before 1996?

(Sergio de Del Castillo): Hi this is Sergio de Del Costello from the Office of Device Evaluation. The guidance will now be in effect for any submission that comes to the house as of the March 12th date of the guidance.

Shannon Scruggs: So any new submissions as of the 12th. Okay.

Sergio de Del Costello: Correct.

Shannon Scruggs: All right. Thank you. That was the only question that I had.

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

(Sandra Aprehenian): Hi. I have a question about single patient reuse devices that was added to the scope of the guidance document, because it was added into the scope but not really addressed within the guidance document itself, except through the process overview in the Appendix.

And so the question is, is the flow chart goes into the risk of cross contamination of the device, and then also if the device could be soiled by body fluids. And it uses kind of vague terms, unlikely or maybe, and so I was

kind of wondering how the agency is going to make those determinations for devices that are specifically labeled as single-patient use.

(Steve Turtill): Hi, this is Steve Turtill. Really, again this harps back towards the way the validation protocol should be designed, and that should be for worst-case scenarios.

So if there's any doubt, you know, that there might be accidental use or just rare occasional use of their being a contamination event occurring, the design of the validation protocols really should be written in such a way that they address the worst case, so that, you know, if there's a contamination event that may occur, it should be included, really, in the design of the validation protocol.

(Elaine Mayhall): That would be a good question that should go directly to the device review division.

(Sandra Aprehenian): All right. Thank you.

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

(Ed Marindola): My question is actually very similar to the last and probably was answered, by the last, but in the scope of the guidance where you talk about reusable devices intended for reuse by a single patient and reprocessed between each use, do you guys define what a use is or is there a definition of what a use is? Is there like a time period to it? Is it...

(Geetha Jayan): We do not define the word use in the guidance, but, you know, a use is a use of the device. Maybe, you know, maybe for certain specific devices if you

have questions, again, you know, please refer the questions to the specific device review division.

(Ed Marindola): Okay. Thank you.

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

(Julia Yay): Hi. I have a question regarding the noncritical devices. It gives examples, like a stethoscope or a blood pressure cuff. I wanted to understand what type of validation would be required for those types of devices, because they don't actually - or my understanding is, they wouldn't actually involve, you know, determining the microbes and soil or validation of those types for this noncritical device. Can you expand on that?

(Elaine Mayhall): The labeling should include instructions for processing any type of reusable device. So even for a blood pressure cuff there should be instructions for cleaning and disinfection of the device, because it could become soiled with patient material.

(Julia Yay): Okay, so there would be an expectation to validate that cleaning. Let's say if it was with, like, an alcohol swab, there would be an expectation to validate the alcohol swab removed the soil from this type of device?

(Elaine Mayhall): Correct.

(Julia Yay): Okay. Thank you.

Coordinator: Our next questions from (Sarah Freedburg). Your line is open.

(Sarah Freedburg): Hi. Thank you for taking our questions and for the presentation. I have a question on criterion states that the instructions should be understandable. One of the recommendations is that we, as manufacturers, include charts, diagrams or pictures that can be posted in work stations.

And while we completely agree that having, you know, a diagram of some of the more complicated cleaning steps or sterilization processed could be helpful to the end user, I guess my question is, expectation wise, for something like a chart or a diagram that's going to be removed from the IEP and placed up on a wall, what level of warnings and cautions would FDA want to be on such a chart or a diagram?

Does it need all the cautions or warnings that would be in the entire IFU, or is it sufficient to put, you know, a statement that the IFU should be looked at to see all the warnings and cautions?

(Elaine Mayhall): I think that this depends on the specific device and what's critical to be on that poster. But again, I think that's a question that's specific to the review division for whatever device you want to ask that of.

(Sarah Freedburg): Okay. Thank you.

Coordinator: Our next question is from Frank Canonica. Your line is open.

Frank Canonica: Good afternoon, this is Frank Canonica at Pentax Medical. I was hoping that you would be able to help clarify a description in Section 8 on the various test types that are used to validate cleaning.

When the guidance states that at least two quantitative test methods should be used, do you mean that for each soil indicator of, say, protein, carbohydrate

and hemoglobin, are you saying that for each one of those types of soil indicators that two quantitative methods should be used to assess residual levels of those indicators?

Or are you saying that only two indicators need be tracked, and for each of those two indicators that only one quantitative method be employed? Or are you saying something different than either of those two descriptions?

Steve Turtill: That would be your second description, not the very last one. But basically you want to know that of the components that are in the soil, that there's at least one test type that addresses each of those components. So for a particular clinical soil, you may have varying degrees of carbohydrates, proteins, or lipid. We just want to know - we would like to see quantitative test data.

For example, one for the protein, one for the carbohydrates. Or if you wanted to include full organic carbon. However you decided on which those two are, a total of two is what we're looking for.

Frank Canonica: Okay, thank you for the clarification. Now that is, from what I understand, that is a change in course from what is typically being employed at the present time. I know that historically, at least for determinations that we have conducted on cleaning, we've been following three markers, namely protein, carbohydrate and hemoglobin.

Is the agency saying now that two markers are sufficient, and if so - which is what I derived from the answer that you just provided. And if only two markers are required where we were normally providing three, which of the three markers should we be providing and on what basis?

(Geetha Jayan): So we are recommending that you provide a minimum of two, and if you use three and provide that information, that's fine. But our recommendation is to provide a minimum of two. Like protein and hemoglobin, or total organic carbon, you know? Any two quantitative markers.

Frank Canonica: Is there any two that are preferential? Is there, say, among protein, carbohydrate, and hemoglobin, is there a particular priority order that the agency has determined - is one more important than the other?

I mean, because if we're going to drop down to two instead of three, we certainly don't want to pick the wrong two. So is there some kind of priority that's been established among protein, carbohydrate, and hemoglobin, as to which one of those three may be omitted from this point forward?

(Geetha Jayan): Whichever marker you pick, it needs to represent the conditions that the clinical, you know the device would be exposed to under clinical use. So if it is exposed to mucus for example, you need to pick the appropriate marker that is relevant to assessing mucus.

So if it is exposed to blood then, you know, hemoglobin is an appropriate marker. So, essentially, we are asking that you pick the soils based on the clinical use of the device.

Frank Canonica: Okay. So again, that would depend on the use of the device, the particular formulation of the artificial test soil that we construct in order to represent that anatomical site where the device is used, and then the prevalent markers from that ATS formulation?

Steve Turtill: So there are several considerations there in the design of your protocol. And in general, we're giving guidance here, but a couple of questions have come up

regarding sample sizes or number of uses or types of soil used and, really, it's important to think it through as best you can to find out the answer, you know, the best way to find the answer to get most meaningful data that you can.

And if you choose to use three markers, or a very large number of samples, it's only going to strengthen your data and give you better answers, more valuable and more meaningful answers.

Another element to that is how you choose those particular markers for those particular soils, it may vary depending upon, you know, what components they are, you know, what percentage of the component they are in the actual clinical soil.

Frank Canonica: Okay.

Steve Turtill: But you may also need to evaluate the degree of strength that they adhere to the surfaces. So some of those components that you mentioned, some of them may be much more tightly binding to the surface and may be more of a problem for cleaning.

So there's not a one answer fits all with these things, and that's why we do, on a number of the occasions, recommend that you contact the lead reviewing branch or division, because they have a little bit better of an understanding of those particular device types.

Frank Canonica: Understood. Thank you very much. One additional follow-up question. As relates to simulated use of the device, again, historically, in simulating the use of the device, we have been employing, you know, approximately ten cycles under the guidance of the agency, and now that we're reading the newly-passed guidance, newly issued guidance, they're making - the guidance makes

a reference to employing a statistically significant number of cycles during simulated use.

My question is, can a device manufacturer anticipate that the number of simulated use cycles that they will be required to perform will now evolve to something other than the standard 6-10 cycles that have been employed previously?

In other words, are you going to have to do some kind of a calculation in which you anticipate for a reusable device that it may be used X amount of times over a given, over its useful life, or under the warranty period or whatever parameter you choose to select, and then run a number of simulated use cycles that somehow relates to that number?

(Geetha Jayan): So I believe this question, you know, the number of cycles would depend upon the complexity of the device and the specific details of the device. So this is a question that you should be asking the review division.

Frank Canonica: Okay.

(Geetha Jayan): They would be able to give you more guidance on that.

Frank Canonica: Okay. Thank you very much. I appreciate it.

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

(Daniel Rubnick): Hi. In this presentation, you mentioned that the cleaning and sterilization are treated independently. So I just wanted to clarify that there's no expectation that every combination of cleaner and disinfection and sterilization process is required to be tested?

(Elaine Mayhall): You should be testing whatever you recommend in the labeling of the device.

(Daniel Rubnick): Yes. So for instance, if we recommend six different cleaners and three different sterilization processes, do we have to test every combination of those? Because that becomes an exhaustive number of tests.

(Elaine Mayhall): Yes. You should do validation testing to validate the cleaning process with anything that you specify in the labeling, and you should definitely do validation of each of the sterilization methods recommended in your labeling.

(Daniel Rubnick): Yes. So we test every method, but we're not required to test every combination? In other words, cleaner one with sterilization method three, and then cleaner one with sterilization method two. You treat them as independent?

(Elaine Mayhall): To validate the cleaning method and the sterilization methods, they have to be validated separately and independently. If you're looking at biocompatibility or compatibility of the device with the processes, that's different.

(Geetha Jayan): And then again, whatever you're recommending in the labeling, that is what you need to test and validation. I mean, you asked a question, I believe, like, cleaning method one with a certain sterilization method. So if that is what you're recommending in your labeling, that needs to be validated.

(Daniel Rubnick): Sorry, it's not clear to me. If we are recommending six different cleaners, and three different sterilization methods, and we test each one independently, that is sufficient?

(Geetha Jayan): Again that depends, you know? If you're recommending six independent cleaners independently and three disinfectants independently, and it does not matter how the user uses them, you can validate each independently.

Then again, it depends on, you know, what specific instructions are you providing in your labeling? Whatever instructions you are providing in your labeling, that needs to be validated.

(Daniel Rubnick): Okay. Thank you.

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

(Charity Hoby): Are there any requirements for a microbial log reduction for each disinfection level such as low, intermediate, or high?

(Elaine Mayhall): There are, if I can remember it right now. It's not specified in the guidance document, you may be able to find it in other guidance documents, such as the one for medical washer disinfectors.

Low-level disinfection would be a six log reduction of four vegetative bacteria: - Klebsiella, Pseudomonas - I can't remember the other ones, but there are four different ones.

And then for intermediate-level disinfection, it would be the six log reduction of each of those vegetative organisms, as well as showing us three log reduction of an appropriate mycobacterium species. And each of those tests should be done independently, separately with each bug. And then with high-level disinfection, you should show a six log kill of mycobacteria.

(Charity Hoby): And so you can't do a cocktail of microbes?

(Elaine Mayhall): It is preferable to test each organism separately. If you can provide justification for doing a cocktail, you can provide that. But generally we've requested that each organism be tested separately.

(Charity Hoby): Thank you.

Coordinator: At this time we are going to be taking our last question. And our last question is from (Gary Secola). Your line is open, sir.

(Gary Secola): Great. Thank you for taking my question. In Section 9, it discusses disinfection or sterilization. And in the second paragraph there's a statement, "validation data should be generated in FDA-cleared sterilizers and with FDA-cleared sterilization accessories, e.g., biological indicators, physical/chemical sterilization process indicators, sterilization wraps.)"

This, you know, typically is done when sterilizing - or, excuse me, validating sterilizers or sterilization processes. And when validating reusable medical devices, specifically Class II devices, typically the biological indicators used for the validation process are not FDA cleared, not all of them.

Most healthcare FDA-cleared BIs is self-contained. So when trying to validate a complex device like an endoscope or some other lumen-type device, you know inoculated threads or even direct inoculum is used. So this statement appears that those types of BIs cannot be used in the validation process anymore.

(Steve Elliott): Hi. This is (Steve Elliott). With regards to that, the intention behind that language is to ensure that the validations are going to be consistent with FDA-cleared cycles and accessories.

If appropriate, it could be acceptable to use biological indicators that have not been FDA cleared, particularly if the resistant characteristics are known and appropriate and the nature of the validation involves something like a direct inoculation or the emplacement on a wire or something like that, that wouldn't be possible with a paper BI or (SCBI).

(Gary Secola): Okay. Great. Thank you.

Coordinator: I turn it back over to your host.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions. If you were unable to ask your question during our question and answer session, please send your inquiries to DICE@fda.hhs.gov. Today's presentation and transcript will be available on the CDRHLearn Web page at www.fda.gov/training/CDRHLearn by Wednesday, April 1.

If you have 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.

Coordinator: This does conclude today's conference call. We thank you all for participating. You may disconnect and have a great rest of your day. Start typing here:

END