Medical Device Sterilization Town Hall: The Value and Use of Recognized Consensus Standards in Premarket Submissions
March 21, 2024

Moderator: CDR Kim Piermatteo

CDR Kim Piermatteo: Hello, everyone, and welcome. Thanks for joining us for our fifth Medical Device Sterilization Town Hall. This is Commander Kim Piermatteo of the United States Public Health Service and I serve as the Education Program Administrator in the Division of Industry and Consumer Education in CDRH's Office of Communication and Education. I'll be the moderator for today.

The FDA is committed to reducing reliance on ethylene oxide sterilization use while ensuring the integrity of the supply chain so that patients and providers have continued access to the sterile devices they need. To meet this goal, FDA continues to take a multi-pronged approach, including regulatory flexibilities, supply chain analysis and mitigation, collaboration, innovation, and communication, including this series of town halls.

I would like to share a few administrative items before we get started today. First, printable slides of today's presentation are available on CDRH Learn. To obtain these slides, you can go to CDRH Learn at www.fda.gov/training/cdrhlearn and select the section titled Specialty Technical Topics and then, scroll down to the subsection titled Sterility. There, you will find the Medical Device Sterilization Town Hall section and a link to the printable slides for today's town hall, as well as materials from past town halls.

Next, please make sure you've joined us through the Zoom app and not through a web browser to avoid technical issues. Additionally, trade press reporters are encouraged to consult with the CDRH trade press team at cdrhtradepress@fda.hhs.gov. Members of national media may consult with FDA's Office of Media Affairs at fdaoma@fda.hhs.gov. And lastly, we look forward to interacting with you today. If you have a comment or question, please wait to raise your hand in Zoom until after the presentation and we transition to this segment.

I now have the pleasure of introducing our presenters for today's town hall. Dr. Lisa Simone, Senior Health Scientist and EtO Incident Lead in the Division of All Hazards Preparedness and Response in the Office of Readiness and Response within the Office of Strategic Partnerships and Technology Innovation, or OST; and Arun Le, Senior Standards Advisor within the Division of Standards Conformity and Assessment, also within the Office of Readiness and Response in OST; and Dr. Ryan Ortega, Regulatory Advisor on the Regulatory Policy and Combination Product staff within the Office of Product Evaluation and Quality, or OPEQ. Thank you all, again, for joining us. I'll now turn it over to Lisa to start today's presentation. Lisa.

Lisa Simone: Thanks, Kim. And thank you for continuing to engage with us in this EtO Town Hall series. Our last two town halls focused on premarket submission expectations for sterility review for new submissions and device modifications. We also talked about the use of guidance documents and master files during premarket review.

Today, we'll expand that discussion to include consensus standards and their value in helping to demonstrate safety and effectiveness, including in premarket review. We'll also discuss how to use standards as part of your submission, the role of our standards program in supporting the advancement of standards, and how you might get involved in the collaborative standards development process.

Recognition, development, and use of standards is part of FDA's multi-pronged approach to ensuring the availability of sterile medical devices. Next slide, please.

Before we get started with our discussion today, we'd like to take the opportunity to answer some questions we received in our mailbox. First question, understanding that no alternative to EtO exists for many devices and none mirrors EtO's compatibility, efficiency, capacity, and throughput, which is critical to infection control and supply availability of sterile devices for patients and providers in the US, can you speak to FDA's view on the role of internationally recognized standards and how that might assist in additional sterilization methods where that is possible?

That is a great question. And as we've mentioned previously, there is no sterilization modality that is directly comparable to ethylene oxide in terms of broad compatibility and capacity. That notwithstanding the potential impact of a range of alternative modalities, taken together, we believe could begin to relieve an overreliance on EtO. And as you suggest, the use of internationally recognized consensus standards is one important avenue towards progress in this area. And as you'll hear more about during today's presentation, FDA strongly supports sterilization innovation through the development and use of FDA-recognized consensus standards or documents, which will further the understanding of these modalities and the development of testing and validation methodologies.

And for the second question, at my company, we've been working to validate ethylene oxide sterilization cycles at lower gas concentrations; however, we've run into roadblocks with long regulatory approvals in Europe. The implications are that it takes us longer to implement the EtO sterilization changes. What might the FDA do to partner with their peer regulatory agencies around the globe to develop alignment on a means of expedited approvals?

Again, thank you for that very timely and increasingly common question. One way that CDRH engages internationally is via voluntary consensus, for example, the standards, development, and recognition that I just mentioned. And this highlights some of the commonality between this question and the previous one. Recognizing some of the roadblocks that you've identified, we've initiated conversations with international partners to understand present barriers and explore where opportunities might exist, especially where significant increases in regulatory requirements are currently in place or might be anticipated.

For example, we've mentioned prior that we've heard FDA flexibilities might not be helpful for multinational organizations without some sort of global regulatory harmonization or reliance effort in place. And we also recognize that different jurisdictions may have different technical requirements.

We continue to welcome conversations on opportunities in this area and we hope that the topic of today's town hall might help foster those conversations, at least in regards to the use of consensus standards. It would also be helpful for us to understand how industry might be collaborating with other regulators or with one another on addressing some of these challenges. This appears to be a continuing area of interest and potential opportunity, so we look forward to hearing more about your thoughts during the Q&A session today or in our mailbox after the town hall. Now, let's get started on today's topic. Next slide, please.

This is the same activity timeline you've seen previously and as a part of today's topic, we'll mention our recognition of three consensus documents in support of medical device sterilization highlighted in yellow. Next slide, please.

For today's town hall, we will describe the value of using consensus standards, including their use in premarket review; describe the principles of standards development and the role of CDRH's Division of Standards and Conformity Assessment, or DSCA in recognizing consensus standards; understand the utility of three recently FDA-recognized sterility consensus documents for regulatory submissions; and describe the value of participating in the collaborative standards development process and how you can help. And as a general note, throughout the presentation, we'll use the term consensus standards as most standards use for regulatory purposes fit this description. Now, I'll turn it over to Arun Le for the first learning objective. Next slide, please.

Arun Le: Thank you, Lisa. I appreciate the opportunity to share with you the important information about the value and use of consensus standards in premarket review. Next slide, please.

Next slide, please.

Consensus standards are valued across all economic sectors and by device developers, conformity assessment bodies, regulators, and users alike, and for good reason. First and foremost, they improve product quality because they rely upon the consensus process and, thus, draw upon the knowledge and experience of a wide range of experts around the world. Standards are much more efficient than relying upon government rules and regulations, which is why the US government directs its agencies to tap into consensus standards whenever possible and not to create unnecessary government standards. By creating a level playing field and clear expectations, standards foster competition and, thus, innovation in product development, which, in turn, drives the availability of new and improved devices for patients we serve.

Manufacturers, in particular, value consensus standards because they reduce burden when multiple regulatory jurisdictions use standards. It makes device development and testing globally more straightforward, thereby enhancing international harmonization. Of course, standards are an integral tool in regulatory practices, and their use advances regulatory science tremendously. Finally, when standards are written with clear testing and acceptance criteria built in, they streamline conformity assessment and device review. Next slide, please.

As I just mentioned, creating standards under consensus principles ensures that the standards reflect the views and expertise of interested stakeholders from across the device community, but consensus means more than that. According to the World Trade Organization, in order to be considered consensus standards, they must be written under these rigorous conditions. First, transparency, all work must be visible and accessible. Second, openness, other's viewpoints are welcomed and considered. Third, impartiality and consensus, individuals approach standards work with an open mind and a goal to achieve consensus. Fourth, effectiveness and relevance, standards must meet an identified and agreed upon need. Fifth, coherence, standards must make sense and be understandable to users. Six, development and dimension, standards development organizations should consider the constraints of less wealthy nations face and facilitate their participation. Next slide, please.

In our industry, the benefits of relying upon consensus standards are so significant that CDRH goes out of its way to encourage it. In fact, we've published a guidance document entitled Appropriate Use of Voluntary Consensus Standards in Premarket Submissions, which is linked below. In the next learning objective, we'll outline how FDA goes about recognizing consensus standards. But first, let's talk about their value in premarket review.

First of all, FDA-recognized standards have FDA's confidence that conformity will support device claims. And when an FDA-recognized standard is cited, a declaration of conformity is included, which generally reduces documentation needed in the submission. With FDA-recognized standards, we expect to ask fewer additional information questions and as I mentioned earlier, standards used by multiple regulators globally means that manufacturers can use the same resource in different countries. When written well, these standards provide clear direction about what FDA expects. For example, ISO 11135 provides recommendations on validation methods for EtO cycles. Ideally and whenever possible, standards should feature clear test methods and acceptance criteria. The result, it potentially reduces extraneous testing. Next slide, please.

So even though citing recognized standards is voluntary, FDA encourages manufacturers to use them in their device submissions. When an FDA-recognized standard is cited in a Declaration of Conformity, or DOC, less information and less documentation may be needed. This reduces burden for both device manufacturers who are compiling the submission and the FDA staff who review it.

Finally, remember that, at its core, a DOC is a communication to FDA, and communications are always welcome. In this case, a DOC makes it easy for us to understand how you used that standard to support your device claims or meet a regulatory requirement. Next slide, please.

A declaration of conformity is a very simple and straightforward document. It attests that the device conforms to all requirements of a standard. And as such, it confirms to FDA that all normative requirements of the standard have been met. If the submitter is declaring conformity to an FDA-recognized standard, a DOC should be included in the submission along with the appropriate supporting documentation if needed. I want to emphasize a DOC to an FDA-recognized standard generally will not require a complete test report. As you know, some complete test reports can be hundreds of pages long and often raise questions that require time and resources to respond to. Please don't send complete test reports if we don't need them. Note that, if a standard is not FDA-recognized, it can still be cited under what we call general use. General use also applies if the device sponsor does not include a DOC when citing a recognized standard. For general use cases, the complete test reports should be included in the submission and will, of course, take time to be reviewed.

A DOC is more simple and straightforward in eSTAR, which is a submission portal that FDA now requires manufacturers to use for 510(k) submissions. We'll have the link to the eSTAR Program at the end of this presentation. And finally, all of this information and more can be found in the important guidance entitled Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices, which is linked at the bottom of this slide. Next slide, please.

Now that we have an understanding of the value of consensus standards, the next learning objective will describe FDA's standards program and how you might engage with us if there is a standard that you feel would be helpful related to your medical device sterilization. Next slide, please.

The Division of Standards and Conformity Assessment, or DSCA, has four main priorities and they are depicted here as a life cycle of standardization. All of these efforts are directed toward our overarching goal to drive and enhance the development and use of high-quality standards that are fit for regulatory use. Standards development manages over 400 experts across CDRH who participate in standards development to make sure standards reflect regulatory needs. Many of these FDA experts are also on what we call Specialty Task Groups, or STGs, which align with specific areas like sterilization, biocompatibility, quality system, and risk management. And to device-specific areas like orthopedics and IVDs. These STGs assess the standards program and provide recommendation of standards recognition and related policy decisions.

The next element is conformity assessment. When standards are formally recognized, our job is to put them to work on behalf of conformity assessment. The ASCA program is an extension and expansion of this function, and its goal is to streamline conformity assessment aspect of device review. So, we encourage you to participate.

Finally, we take the experience we gain about standards use in supporting their scope, how they use to evaluate the performance, and determine whether revisions are needed to keep up with postmarket data and emerging technologies. Next slide, please.

The term recognition has a very specific meaning at FDA. Recognition is FDA's formal identification of a standard to which it is appropriate for device manufacturers to declare conformance in order to satisfy part of premarket review requirement. As I noted earlier, when manufacturers cite an FDA-recognized standard, they should submit a declaration of conformity in their submission, which generally reduces the amount of supporting documentation that will be required. And manufacturers can easily nominate standards for formal recognition, and we hope you will. FDA recognize all or part of a standard. And to be transparent, we publish our reasoning or rationale for each recognition decision. These decisions can be found in our Recognized Consensus Standards Database, which is available to everyone. The image on the right is a screenshot of the recognition database. There is a database for standards we specifically choose not to recognize.

And finally, we keep an eye on standards and revisions. This way, we know when to update our recognition database or even when to withdraw standards that are no longer suitable for recognition. The guidance, recognition, and withdrawal of voluntary consensus standards contains greater detail and is linked here at the bottom. Next slide, please.

These are steps of FDA when they take on, when they receive and acknowledge a recognition request. First, the standard staff begin the consideration process, then convene the appropriate STG to formally review and to offer recommendation to DSCA. The standards program makes the final decision to recognize or not. And if we decide to recognize the consensus standard, either complete recognition, which is preferred or in part, we'll state it in the extent of recognition. In making these decisions, standard staff, and STG members, of course, rely upon scientific, technical, and regulatory factors. Next slide, please.

FDA is committed to responding within 60 days of the request and sends the decision including the rationale back to the requester. The recognized standard is then added to FDA's recognized Consensus Standards Database. And an official recognition follows later with publication in the Federal Register. It's important to note that manufacturers may cite a recognized consensus standard as soon as it appears in

the Recognized Consensus Standards Database. So, no need to wait until the Federal Register is published. Next slide, please.

When a standard is formally recognized, FDA publishes a Supplementary Information Sheet, or an SIS, in the database. It is a valuable resource for device manufacturers that contain a variety of information. I draw your attention, especially to the scope, extent of recognition, a transition period if there's one, and any guidance or documents that will have relevant information for using the standard. And now, I'll turn it over to Dr. Ortega who will dive into newly recognized documents that support sterilization. Thank you.

Ryan Ortega: Thanks, Arun. Now, for our next topic, I'll talk about some recently recognized consensus documents and how they might be used in submissions. In our last learning objective, Arun ended with the description of some of the information about our recognition of consensus standards that we provide in the SIS for a standard. I'll build on that using the newly recognized VHP validation standard as an example. FDA recently recognized this new standard, as well as two Technical Information Reports, or TIRs, related to device sterilization that we think are helpful resources for considering alternatives to ethylene oxide or for making changes to sterilization processes. I'll briefly describe some of the high-level content in these documents and also present some possible scenarios for using them in order to add value to regulatory submissions or using them to help justify sterilization methods or changes. Next slide, please.

So, let's get into some specifics. ISO 22441 is a relatively new standard, and we recognized it in 2023. This is the first new modality-specific sterilization validation standard recognized by FDA in many years, so we're pretty excited about it. It's got normative directions for the validation, monitoring, and control of vaporized hydrogen peroxide sterilization. Now, as a recognized consensus standard, a DOC can be included in a regulatory submission. Like Arun said, this can reduce the amount of supporting documentation needed in a submission. It can simplify the review process. And it can also provide clarity about the methods used to validate and control a sterilization process.

In a previous town hall, we described how making a DOC to a recognized standard in a 510(k) generally means that summary information can be provided for the sterilization method per our 510(k) sterility guidance. Now if making a DOC in a PMA or another type of premarket submission, we generally would expect more sterilization information than in a 510(k). This is one of those cases where full test reports may be needed to go along with the DOC.

We talked about our expectations for sterility test reports in our third town hall, but just to refresh your memory a little bit, in terms of sterility, a full test report will generally include things like installation qualification, operational qualification, performance qualification, et cetera. And this isn't an exhaustive list, but it gives you a sense of how the standard can be used, not just to support the technical aspects of establishing a process but also how it can provide a useful framework for identifying the type of info that can be helpful to provide in premarket review in cases where a full test report might be needed.

Ultimately, if you have specific questions about both the type and amount of sterility information to provide for your device, I definitely encourage you to reach out to the review division for your specific device with our Q sub process.

The regulatory utility of this consensus standard and many standards like it can even go beyond using a declaration of conformity. For example, ISO 22441 has recommendations on things like selecting microorganisms for process validation, sensor and indicator placement for monitoring, and it also describes different validation methods for defining the sterilization process like overkill validation, the BI bioburden based method, and methods using the native product bioburden for validation. This technical content can be helpful for providing justification and support in a regulatory submission for the methods used in process validation. Next slide.

Now, when standards are recognized and SIS is generated that describes the standards recognition, this is an example of the SIS for the newly recognized ISO 22441 standard. Like Arun described, it shows information for the standard itself like the scope, as well as the extent of FDA's recognition or rationale for the recognition and any supportive documents or information that might be useful for understanding and using the standard. Again, we definitely encourage you to consult these resources when you're using the standard. And you can see, from this example in the SIS, that, for ISO 22441, we did a complete recognition of this consensus standard.

And we know, from our experience working on this standard and from our experience with health care hydrogen peroxide sterilizers, that there can be different approaches to cycle designs for vaporized hydrogen peroxide. And there can also be differences in how impactful different process parameters can be with respect to controlling the process and reaching the appropriate sterility assurance level. This is why we included a note in the SIS for this standard where we encourage you to come talk to us using our pre sub process if you have questions about our regulatory expectations for VHP process monitoring and control for your specific device; especially if you're considering things like parametric release.

One of the main things I'd really like for you to take away from this is that we really are ready to work together with you in order to further the development and utilization of this and other alternatives to ethylene oxide. Next slide, please.

Before I talk about TIR17 specifically, I would like to briefly explain some of the differences between the consensus standard and a Technical Information Report. A standard may provide normative guidance and directions for an approach to things like testing, test methods, practices, manufacturing techniques. You could make a DOC for a standard. On the other hand, a TIR may serve as an interim statement by a committee working to develop standards, it may provide some additional guidance for using a standard, or it could present useful scientific or technical information on a topic. While you wouldn't necessarily make a declaration of conformity to a TIR, you could cite general use of a TIR in a regulatory submission and describe how you utilized it in device testing or development.

Now onto TIR17, this is titled Compatibility of materials subject to sterilization and this TIR is from the Association for Advancement of Medical Instrumentation, or AAMI and it has general information about the compatibility of materials subjected to different sterilization methods. It includes some very useful material compatibility tables that are helpful for understanding how a specific modality might impact device materials.

We understand that this is generalized information and that there would still need to be device-specific assessments of material compatibility made in order to select and validate a sterilization process for a specific device. Luckily, this TIR also supports this device-specific work with considerations for material testing and functionality testing.

There's potential regulatory utility in citing the general use of this TIR. It could be useful in supporting a discussion of material selection or device functionality following terminal sterilization. It could help support the selection and development of a sterilization process for new devices. But it's also useful for considering if a change from one modality to another might be feasible, at least from a material compatibility perspective.

Also, this TIR isn't just for sterilization experts. We know it can be a challenge to develop a sterilization process for some devices if sterilization wasn't considered during device design. A tool like TIR17 can be useful for people working at the R&D phase of device development to aid in material selection and device design in order to help ensure that the device is designed to be sterilizable. It can facilitate an end-to-end approach to device sterility and support collaboration between those who are developing the device and those who are responsible for the microbial control and sterility. Next slide.

Now, I'll talk a little about AAMI TIR104, which provides guidance on transferring health care products between radiation sterilization sources. Now radiation sterilization, it's the second most common method of terminal sterilization for devices. And gamma radiating material is the most common source for radiation sterilization. But its capacity isn't infinite. We've heard that the logistical considerations for acquiring and transporting gamma radiating material can be complex and the supply of material can potentially even be impacted by geopolitical events. This TIR is important because it supports transferring medical devices from gamma to other radiation sources like electron beam or x-ray. And it supports changes from one irradiator to another, for example, moving from a gamma process at one site to a gamma process at another site. It gives helpful technical information about potential differences between radiation sources and helps support an assessment of the similarities. It also has recommendations for establishing the different doses that are critical for validating and controlling a radiation sterilization process. And it has guidance for how to appropriately document and support a change, which is very useful from a regulatory perspective.

Like TIR17, TIR104 has value both from a technical and industrial perspective and from a regulatory perspective. Citing the general use of this TIR in a submission can be helpful for providing justification and support for a change from one radiation source to another. For example, a manufacturer might walk through the relevant sections from the TIR in their regulatory submission and that could help us understand why they did what they did when changing radiation sources. I think this is significant because the overall sterilization capacity for non-ethylene oxide methods like radiation, it's an important component of the medical device ecosystem and the sterile device supply chain. Increasing or enhancing the capacity for alternative methods can help support shifting devices away from ethylene oxide where that's possible.

So now one final thought on TIRs. We don't recognize them as often as we do consensus standards. They're not the same as consensus standards with respect to making a declaration of conformity; however, the recognition of these TIRs emphasizes that we're exploring every option, every opportunity to be creative in how we're supporting the development of alternatives to ethylene oxide within our regulatory purview. The considerations provided in these TIRs are timely for the moment we find ourselves in. We think recognizing them helps us support our shared goals for finding alternatives to ethylene oxide and it facilitates our regulatory decision making. Next slide.

The last thing I'd like to touch on briefly are some final thoughts on participating in the collaborative standards development process. Next slide.

As mentioned throughout the whole presentation, standards really do help both manufacturers and regulatory jurisdictions. They help simplify the regulatory review process and they create sets of shared standard expectations for critical parts of the device development, testing, and manufacturing processes.

I hope we've helped emphasize how valuable consensus standards really can be and so, here's some thoughts for how you can help contribute to the value that consensus standards provide. And this is really the call to action because, essentially, what it comes down to is that the standards development process needs you. Standards development, it's really a collaborative process and it relies on the expertise and experience of folks who work in relevant fields for any given standard.

New standards need to be based on good science and good engineering. As the body of science for new sterilization methods expands, we get closer to being able to develop standards for these new methods. And there are several standard's bodies that support working device sterility, and they have multiple mechanisms for putting out different types of consensus documents. If you see a gap that could be filled by a new standard or another type of consensus document, consider proposing one. And once standards are in development, it takes a concerted effort from a dedicated group of subject matter experts to write, revise, and finalize it. If you or your organization have expertise in a certain area that's being worked on by standard's organizations, we definitely encourage you to get involved.

Finally, if there are consensus standards out there that FDA hasn't recognized and you think it would be useful for the regulatory process, whether through being able to make a DOC or through their general use, we encourage you to consider proposing them for recognition. Next slide.

So, these next two slides include some of the resources mentioned earlier in the presentation along with the full URLs that you can access after the presentation.

Now to summarize, we've talked about the advantages of using consensus standards in regulatory submissions and how they're used in regulatory review. We talked about how CDRH's standards program promotes the development, recognition, and use of consensus standards and device development. We've talked about three recently recognized consensus documents and how they can assist industry in adopting new sterilization methods and also how participation in the development of standards is a collaborative effort and it promotes important inclusivity and transparency principles to crowdsource the best possible standards. Next slide.

Finally, before we open up the discussion in the Q&A, I'm very excited to announce that our next town hall on April 29 of this year where we plan to share feedback that we've received from you about potential town hall topics going forward and also our thoughts on some additional town hall formats to increase our interactions with you. So please continue to send us your feedback. Information about the town hall series can be found at the link here. Now, I'll turn it back over to Kim to move us into the next phase of the discussion.

CDR Kim Piermatteo: Thanks, Ryan and thank you, Lisa and Arun for your presentations today. At this time, we'll now transition to our interactive segment for today. And joining our presenters for this

segment is Dr. Terry Woods, Director of the Division of Standards Conformity and Assessment within the Office of Readiness and Response in the Office of Strategic Partnerships and Technology Innovation, or OST, and Dr. Aftin Ross, Deputy Director of the Office of Readiness and Response within OST as well. So, thank you both for joining us today.

I'd now like to go over how we will manage this segment and a few reminders before we begin. First, to ask a question or provide a comment, please select the Raise Hand icon, which should appear on the bottom of your Zoom screen. I'll announce your name and give you permission to talk, then when prompted, please select the blue button to unmute your line in Zoom and identify yourself and your organization and then ask your question or provide your comment.

If you have a question, please remember to limit yourself to asking one question only and try to keep it as short as possible. After you ask your question or provide a comment, please lower your hand in Zoom, and if you have another question or comment, please raise your hand again to get back into the queue, and I'll call on you as time permits. As we wait to receive some of your questions and comments today, I'd like to ask our presenters and additional panelists a few questions.

The first question I'd like to direct to Aftin. Aftin, the question is you've shared that FDA continues to receive information about current sterilization challenges. Is there any additional information related to the use of standards that might be helpful?

Aftin Ross: Yes. We continue to welcome your thoughts on today's topic during today's question and answer session or via our mailbox shown on the slide. Please note that any information you provide to us via the mailbox is considered confidential and proprietary and would be protected in accordance with applicable law. And we would only use it to augment our understanding of the current challenges and successes.

With that in mind, we're interested in additional opportunities where consensus standards may be helpful in reducing EtO use and/or switching to other sterilization methods. For example, what standards might be considered for recognition or development? Second, what standards' workgroup might be needed to advance sterilization innovation? Third, what are the major challenges to establishing these work groups or standards? And finally, if you could suggest one sterilization-related action for FDA to consider, what might it be? Thanks, Kim.

CDR Kim Piermatteo: Thank you, Aftin. Alright, next, I'm going to come to Terry. Terry, the question is, how can we learn more about new consensus standards recognition decisions?

Terry Woods: Hi, Kim. Thanks for the question. We announce our consensus standards recognition decisions in CDRH New. And you can subscribe to the CDRH New mailing list by searching for C-D-R-H N-E-W, that's CDRH New to find our news and updates web page. Then, click the Subscribe button to view the subscriptions that are available, like CDRH New. In addition, our Division of Standards and Conformity Assessment, or DSCA, will soon publish our first newsletter, so, keep your eye out for our newsletter. That will also feature new recognition decisions and you will hear about the new newsletter in CDRH New. So, back to you, Kim.

CDR Kim Piermatteo: Thanks, Terry. Alright, before we go to our first live question, I'm going to ask Lisa question before we do that. So, Lisa, the question is, during some of the previous town halls, you've

shared topics where FDA is interested in receiving feedback. Do you have any additional topics of interest today?

Lisa Simone: Thanks Kim. Of course, we do because we're always looking for input from our stakeholders. Many of the questions we've received from you involve situations or challenges where additional information would be incredibly important for our understanding and for potential next steps. For example, maybe you recall, in Town Hall 2, we asked those of you with successes in shifting to alternative modalities to share your approaches and challenges. In Town Hall 3, we asked those of you who considered shifting from paper labeling to eLabeling or those who had already shifted to also share your strategies and challenges. And we're still requesting input on those two topics, but for this town hall, we're asking you to follow up on the question I shared at the start of today's event, the idea of international alignment or harmonization or reliance. This is an area where your experience and suggestions would be incredibly valuable. So please consider sharing your feedback today live or through our email address. Thanks, Kim.

CDR Kim Piermatteo: Thank you, Lisa. Thank you all for answering those previously submitted questions. We will now hear from our first live audience member, Byron. Byron, I have unmuted your line. Please unmute yourself and ask your question or provide your comment.

Byron Lambert: Thanks very much. Byron Lambert with Abbott. Again, enormous thank you for the FDA and proactively and diligently trying to support the industry in helping us move to alternatives to ethylene oxide sustainable technologies and the rapid response of recognizing standards and your support of TIR17 on material compatibility. Material compatibility is a linchpin to be able to change technologies and your active support on that and multiple ways participating, and potentially with collaboration initiatives in the industry, are just very much appreciated. And, again, highlighting the change in modalities and radiation was also helpful.

I wanted to provide just a note relative to your request for information about the potential of new standards activities or guidance. And there's something very current. And on Monday of this coming week, AAMI has the Sterilization Standards Week. And at the opening plenary, there's going to be a brief discussion of a new work item proposal related to giving guidance for alternative sustainable sterilization technologies. And this work was actually initiated five or so years ago and the industry leaders that were doing and it got sidetracked and also, the VHP work that ended up with ISO 22441 kind of took the front seat. And that progressed in one of the working groups that was considering this. But we're going back and resurrecting initiatives, along with some of the sterilization vendors that are the major ones that are working on that. And the proposed scope, and this is in discussion, we've been socializing it with different working groups, is to give guidance on sustainable gas, alternative gas sterilization modalities.

So VHP is already covered. So, it would be NO2 and CL02 and other modalities that they're to provide guidance on nuances of how to do validation. So, these modalities have the ISO standard 14937, the general criteria standard, but what are the specific nuances of the modalities that guidance would be helpful? But then, one of the novel aspects is we're proposing to extend that into BI development. And what do we need to have or guidances for the BIs that are used for these technologies and then, also, into the residual guidance? So, in terms of developing guidance for companies and assessing residuals linked to their biocompatibility, what guidance is there? So again, this is very early discussions, but I'm

confident the FDA will be actively involved in that but just wanted to bring that to your and others attention.

CDR Kim Piermatteo: Thank you, Byron. Does anyone from the group want to comment or respond to what Byron is saying at this time?

Alright.

Lisa Simone: Hi, Kim. This is Lisa. I know that Byron didn't have a specific question, but he's highlighted some really terrific areas that we have been discussing internally as part of this entire exploratory process. Some of them are very aligned with conversations that we've been having, potential subtopics for future town halls. So, I would say, Byron, thank you for that really valuable comment and please stay tuned because we're aligned with a lot of you are thinking and really appreciate the positive feedback that you've given to us today.

Byron Lambert: Very good.

CDR Kim Piermatteo: Great. Thank you, again, Byron. And thank you, Lisa. Our next question is coming from Mac. Mac, I have unmuted your line. Please unmute yourself and ask your question or provide your comment.

Mac McKeen: Thank you. Yes, Mac McKeen from Boston Scientific. I have a question regarding whether FDA has or will consider combining recognized consensus standards with the PCCP process going forward. I know that's sort of being developed within the agency and how to implement various PCCP protocols and processes, but just interested if there's any thought given to that regarding using PCCP to implement on an ongoing basis these sterilization changes.

CDR Kim Piermatteo: Thank you, Mac. I'm going to turn it over to Ryan to provide your response.

Ryan Ortega: Thank you for that question. And this isn't the first time we've heard the idea pitched to potentially having some intersection between sterility and PCCP. And I think the regulatory underpinnings of what PCCP is and what it can be used for, I do think sterilization is potentially within the scope and I can only imagine that being able to leverage recognized consensus standards would make that easier than if there weren't a standard available to reference and to have that shared language and shared understanding of process.

For specific ideas of how this might be used, though, I would definitely recommend reaching out to, if you've got a specific device in mind, reaching out to that team that reviews that device in a pre submission to talk about exactly how a PCCP might be valuable in your specific case, what it might look like, what sort of changes might be appropriate. And the reason why I think a pre sub, in particular, could be really useful here is that PCCPs are still relatively new. We're still working to understand what it looks like and how it works in a lot of different use cases. So having that early interaction, particularly if both the review staff and maybe some of our more programmatic or regulatory type staff can be involved, that lets us give you our best feedback once we consider what you're thinking about. And so that's what I would recommend and some of the thoughts on the intersection of sterility and PCCP.

CDR Kim Piermatteo: Great. Thank you, Ryan and thank you, Mac, for your question. Our next question is coming from Ganesh. Ganesh, I have unmuted your line. Please unmute yourself and ask your question or provide your comment.

Ganesh, are you able to unmute your line?

Alright, Ganesh, if you still have a question, I'm going to lower your hand, but please, raise it again, and then we will call on you as time permits.

I'd like to turn it back over to Arun or Terry to answer this question. We previously received a question that was, what happens when a new version of an FDA-recognized consensus standard is published? So, Arun or Terry, would you like to provide a response?

Terry Woods: Sure. This is Terry. I can answer that one. When a new version of a standard is published, the same Specialty Task Group, or STG, that considered the recognition of the old standard will review the new version for recognition. And again, we go through the same recognition process where we consult with the liaison representatives, with internal subject matter experts, and with CDRH management to determine whether the standard should be recognized. The STG makes a recommendation to the Division of Standards and Conformity Assessment and then, we decide whether the new version will be recognized or not. Sometimes, depending on the standard, a transition period might be assigned during which manufacturers can issue a declaration of conformity to either version of the standard. And as with all the standards that you use, please check the Supplementary Information Sheet, or the SIS sheet, that is publicly captured on our website for details about the transition periods and other information that can be useful to your use of a particular standard.

CDR Kim Piermatteo: Great. Thank you so much, Terry. Alright, I'm going to circle back to Ophelia. Ophelia, I have unmuted your line. Please unmute yourself and ask your question or provide your comment.

Ophelia Biggs: Hi. Can you hear me?

CDR Kim Piermatteo: Yes, we can.

Ophelia Biggs: Thank you. Thank you so much for this very helpful town hall. So, here's my question. In situations where FDA decides to not recognize a standard related to sterilization and there is no existing guidance pertaining to this topic, how does FDA ensure that their requests for additional information in premarket reviews have a strong scientific basis?

CDR Kim Piermatteo: Thank you, Ophelia, for your question. So, I was thinking Ryan,

Ryan Ortega: Yeah.

CDR Kim Piermatteo: Go ahead.

Ryan Ortega: I can maybe handle the review and scientific piece of this. And if there's a standards piece involved in the non-recognition, definitely welcome a follow-up from my colleagues in standards.

But as far as ensuring that the regulatory review and any request for information are based in science, there's a couple of maybe internal mechanisms and ways that we do that. I think there's a decent amount of machinery behind the scenes within our group of subject matter experts that's probably useful to know about here.

One, there's a whole lot of internal coordination and collaboration that goes into sterility review in CDRH. For example, we've got something called our Sterility Focal Point Program. This is an internal group that we use to ensure review consistency in the area of sterilization and also to share the latest and greatest in terms of scientific and technical information about different sterilization methods, including ones where maybe there's not a recognized consensus standard for that modality.

So, it's a group of technical sterilization subject matter experts from every review office, the OPEQ Immediate Office, and our Office of Science and Engineering Labs. And this group, again, regularly meets to talk about not just the science but also our review practices. And so, this allows us to share some of our experiences across the offices and come to consensus on any new or particularly challenging topics. These focal point representatives are also responsible for sharing information and sterility review practices within their different offices. And it also participates in some training for reviewers.

In addition to that, we also have a bigger community of practice for sterility topics. We've got our ethylene oxide Tiger Team that we introduced in the second town hall. This also plays a role in bringing together review staff for a lot of different topics. So there really is a lot of internal coordination and knowledge sharing that goes on behind the scenes for sterility reviews, again, including those methods where there's maybe not necessarily a sterility standard to refer to, but there is information about review experience, technical and scientific literature that shared within the sterility reviewer community in CDRH.

Ophelia Biggs: Thank you.

Terry Woods: Hi, and this is Terry. I can also chime in a little bit, Ophelia. If it's a standard you're talking about that we haven't recognized and that you think would be useful for supporting device submissions, you can always ask that we consider that standard for recognition. If you go to cdrhstandardstaff@fda.hhs.gov, you can request that we recognize a standard that we haven't recognized yet. Thanks.

Ophelia Biggs: Thank you. That's helpful. Thank you so much.

Ryan Ortega: And actually, before we move on to the next one, I also want to mention there is the general requirement standard for sterilization. That's an ANSI AAMI ISO standard 14937, I think maybe Byron mentioned it. And so that is a recognized consensus standard that is intended to generally apply to sterilization processes. So even if there isn't a modality-specific standard that can be referenced, that general standard is a really good scientific and technical underpinning for device sterilization in general.

Ophelia Biggs: I appreciate it. Thank you for your guidance.

CDR Kim Piermatteo: Thank you, Ophelia. And thank you, Ryan and Terry, for your responses. Alright, at this time, I'm going to open it up to any other questions from our audience. Please raise your hand in Zoom, and we can call on you. I'll give it another minute and see if anybody has any questions.

Alright, seeing no more raised hands, we will go ahead and move to close our town hall for today.

So, thank you all again for joining us. That will wrap up today's town hall. And we thank you for your participation. At this time, I'd like to turn it back over to Lisa to provide her final thoughts.

Lisa Simone: Thanks, Kim. And thanks, everyone, for joining us today for our town hall and sharing your questions and your comments. We really appreciate the robust discussion. We had some great comments and discussion points related to industry activities and collaborative initiatives, some recent activities surrounding resurrecting initiatives and looking for opportunities to provide guidance on sustainable gas alternatives, leveraging recognized consensus standards with predetermined change control plans, and also the value of FDA's Sterility Focal Point Program and other internal coordination to ensure that the documentation provided in the absence of a specific consensus standard is considered.

So, we hope that you had a great opportunity to learn more information about the value and use of consensus standards. Thanks for attending and now, I'll turn it back over to Kim.

CDR Kim Piermatteo: Thank you, Lisa. So, as I mentioned earlier, printable slides of today's presentations are currently available on CDRH Learn at the link provided on this slide under the section titled Specialty Technical Topics and then the subsection titled Sterility. A recording of today's town hall and a transcript will be posted to CDRH Learn under the same section and subsection in the next few weeks. And a screenshot of where you can find these materials on CDRH learn is provided on this slide.

Also mentioned earlier, if you have additional questions or comments about today's topic or presentations, as well as if you have a comment or question for a future town hall, please email medicaldevicesterilization@fda.hhs.gov. If you have general questions about today's town hall, feel free to reach out to DICE at dice@fda.hhs.gov.

You can find a listing of all of our upcoming town halls, as well as other CDRH events via the link provided on the bottom of this slide at www.fda.gov/CRDHwebinar. This link will actually forward you to our CDRH events page. Note the direct URL for the CDRH Events page is www.fda.gov/CDRHevents.

And lastly, as Ryan mentioned earlier, we hope you're able to join us for our next Medical Device Sterilization Town Hall, which is scheduled on Monday, April 29th from 1:00 to 2:00 PM Eastern Time.

Thank you all again for joining us. This concludes today's town hall. Have a nice day.

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