Medical Device Sterilization Town Hall:
FDA Activities and Challenges in Reducing Reliance on Ethylene Oxide (EtO)
January 26, 2024

Moderators: Elias Mallis and Joseph Tartal

Elias Mallis: Hello, everyone, and welcome to today's town hall. This is the second in our series on the topic of medical device sterilization. Thanks for joining us today. I'm Elias Mallis, Director of the Division of Industry and Consumer Education in CDRH's Office of Communication and Education. And I'll be your moderator for today's program.

As we get started today, I wanted to share a few administrative notes with you. First, printable slides for today's presentation have been posted to CDRH Learn. So if you'd like to follow along with us or take notes, you can go to CDRH Learn, click the main section, Specialty Technical Topics, and then subsection titled Sterility. We've set up a new section titled Medical Device Sterilization Town Hall Series. And as we hold more of these sessions, we'll add links to the slides, then the transcript, and recording for your future reference. I'll repeat this information at the end of today's program as well.

Number 2, make sure that you've joined us through the Zoom app and not through a web browser. This is to help avoid any technical difficulties or issues during our Q&A session.

Number 3, trade press reporters are encouraged to consult with the CDRH Trade Press team at CDRHTradePress@fda.hhs.gov. And members of national media may consult with FDA's Office of Media Affairs at FDAOMA@fda.hhs.gov.

And finally, we're eager to interact with you today. If you have a question or comment, please wait until we transition to our interactive segment that follows the initial presentation.

It's my great pleasure to introduce you to our presenters for today's town hall. Dr. Aftin Ross, Deputy Director of the Office of Readiness and Response from the Office of Strategic Partnerships and Technology Innovation, or OST. Dr. Ryan Ortega, Regulatory Advisor on the Regulatory Policy and Combination Product Staff from the Office of Product Evaluation and Quality, or OPEQ. Dr. Lisa Simone, Senior Health Scientist, and Lieutenant Commander Scott Steffen, Senior Program Management Officer-- both are EtO incident leads and come to us from the Division of All Hazards Preparedness and Response in the Office of Readiness and Response in OST.

Thanks again for joining us. I'll turn our program over to Aftin to get us started today.

Aftin Ross: Thank you for joining us today for the second town hall on medical device sterilization. We had a wonderful interactive Q&A session last time and are looking forward to doing so again today. Last time, we asked for you to send questions or suggestions for future town halls to our Medical Device Sterilization mailbox.

Before we get started with our discussion today, we'd like to take the opportunity to share some questions and comments we received in our mailbox after our first town hall on January 10th. These questions and comments fall into three main buckets-- the sterilization of combination products, Established Category A and Established Category B sterilization methods, and future town hall topics.

Regarding combination products, first, I'll start by saying that our goal is to provide a CDRH perspective on sterilization topics for medical devices where CDRH is the lead review center. If you have specific questions about CBER review devices, or CBER or CDER lead combination products, we recommend you reach out to the appropriate review team or division within those centers that review those products.

Second, sterilization of combination products can be complex and often comes down to unique product specific considerations. We understand that manufacturers take different approaches to sterilize these devices and, as such, validating at multiple sites, or even with multiple modalities. In general, our primary consideration when reviewing sterilization for CDRH led devices is ensuring that the sterilization process is validated and controlled at whichever site or sites are implementing the process and to ensure that the terminal sterilization process renders a safe and effective sterile device. That said, validating multiple sites or multiple methods of sterilization for premarket review may help increase supply chain resiliency by mitigating potential impacts from the loss of sterilization capacity.

We also received a question about, what makes a sterilization method an Established Category A versus Established Category B, or novel method, within a 510(k) submission? This categorization scheme is described in our recently updated 510(k) sterility guidance. We plan to go over this categorization and the distinction between them in detail at our next town hall on February 7th.

In the meantime, we want to clarify that this guidance includes the modalities that we are aware of that currently meet our understanding of what makes an Established Category A method. Specifically, these are methods that have a history of safe and effective use, as supported by sources like scientific and technical literature, premarket submission review, and inspections. These methods also have FDA-recognized consensus standards for their validation use. We encourage you to stay tuned for future town halls, where we'll discuss each category in greater detail.

With regard to future town hall topics, we received suggestions such as exploring how to validate sterilization methods that do not have a modality-specific standard, the role of internationally recognized standards in medical device sterilization, and sterilization process optimization, to name a few. We are discussing premarket sterilization review expectations in our Feb 7 town hall, and will be discussing standards in a future town hall. We are also exploring how we might incorporate some of these other topics in the future.

In the interest of time, we'll save questions or comments we've received in the last day or two for the next town hall. Feel free to continue to email us directly or share during the Q&A session at the end of today's presentation. I'll hand it over to next presenter.

Alright, so let's talk a little bit about today's learning objectives. Today's town hall will build upon some of the information presented in the last town hall. We'll start with the 2019 Advisory Committee recommendations and share FDA's early actions to mitigate the impact of the potential loss of EtO sterilization capacity in the U.S.

We'll also describe FDA's forward-leaning approaches with the creation of our EtO Tiger Team and capture FDA's understanding of the opportunities and challenges to using alternative sterilization modalities. Finally, we'll talk about more recent and forward-looking activities to reduce overall EtO reliance within the medical device industry while maintaining a resilient supply of sterilized medical devices. Next slide, please.

We introduced this activity timeline at our January 10 town hall. Any content highlighted in yellow is content that will be touched upon during today's town hall. Now I'll turn it over to Dr. Ryan Ortega.

Ryan Ortega: Yeah, thank you, Aftin. And hello, everyone. So our first learning objective, I'd like to talk about some of our early activities and some of the recommendations that we received from the advisory committee meeting back in November in 2019. One of our very first activities following the Seal Order issued to the sterilization facility in Willowbrook, Illinois, was to think about how we might support innovation for medical device sterilization.

One way we've partnered with stakeholders to support sterility innovation is through our innovation challenges. On July 15 in 2019, we announced two innovation challenges for medical device sterilization. And then shortly after the advisory committee meeting, we announced-- that was on November 25, 2019-- that we had received 46 applications and selected 13 for participation.

The goal of our first challenge is to identify safe and effective sterilization methods or technologies for medical devices that don't rely on ethylene oxide. The challenge stated that these methods should be compatible with a large cross section of materials used to manufacture medical devices, packaging materials, and sterile barriers. They should have the potential to be scalable and allow for sterilization of large volumes of medical devices, which is really important for industrial-scale use of these processes. For this challenge, five applications were selected which represented a variety of methods and technologies.

Now for the second challenge, the goal of the second challenge is focused on developing strategies that reduce ethylene oxide emissions from the sterilization processes that still use ethylene oxide. Eight participants were selected with a variety of strategies, strategies like create a cycle design, or improved abatement strategies for the sterilization chamber exhaust gas.

Next, I want to talk a little bit more about the recommendations that we received from our committee meeting back in 2019. In our first town hall this year, on January 10, we touched on some of these key discussion points from the advisory committee meeting. If you missed it, I definitely encourage you to go back and listen to the recording or view the transcript. This slide shows some key recommendations and advice from the panel members, some of which I'll go over now and we'll also revisit throughout today's town hall.

One piece of feedback we received from the panel was to continue to communicate and work collaboratively with our industry stakeholders and to look for new opportunities to address sterilization-related challenges together. For example, there's been ongoing work on the innovation challenges over the past several years since the committee meeting.

One recommendation we received was to consider incentive structures that could help catalyze ethylene oxide activities, for example, how we might reduce the regulatory burden for firms that are working to take positive steps to reduce their ethylene oxide use. And I'll talk later about Master File Programs that we established in light of this recommendation.

Another recommendation was to consider a risk-based Sterility Assurance Level, or you might have heard the term SAL, for some medical devices where this would be appropriate. We also heard

recommendations to reduce or remove paper labeling as a means of reducing ethylene oxide usage wherever possible. This is important because paper is an absorber of ethylene oxide. We heard recommendations to explore alternative sterilization modalities to reduce ethylene oxide use. And this would also increase overall sterilization capacity in the U.S.

We heard to leverage or develop standards to advance alternative sterilization methods, work with other government agencies at both the federal and state level. And we also heard to continue our partnerships with industry for novel solutions that reduce ethylene oxide usage, and also those solutions that can enhance our ability to respond to device shortages.

Now on to some of our Master File Pilot Programs. We developed these sterilization Master File Pilot Programs to help ensure that patients have access to safe medical devices, and also to encourage new, innovative ways to sterilize devices that can reduce the potential impact of ethylene oxide on the environment and on public health.

On November 25 in 2019, we announced our Ethylene Oxide Sterilization Master File Pilot Program. This is for PMA devices. This first pilot was really a direct result of the advisory committee meeting recommendations for incentive structures. And we developed it to reduce the regulatory burden for sterilization changes.

This is a voluntary program. And it's intended to allow companies that sterilize single-use medical devices using fixed-chamber ethylene oxide to submit a master file when they are making certain changes between their sterilization processes or facilities where these changes reduce the ethylene oxide concentrations used to sterilize medical devices.

Under this pilot, PMA holders of Class III medical devices can reference the master file submitted by their sterilization provider in a post-approval report rather than submitting a PMA supplement if they're within the scope of the accepted master file and making a covered change. There are currently five master files accepted into this first pilot program, meaning that any of these five master files can be referenced by a manufacturer of a PMA approved device within the scope of that master file in an annual report rather than in a PMA supplement for a supported sterilization change.

So then due to the success of that first pilot program, on May 20 in 2022, we announced our Sterility Change Master File Pilot Program for sterilization changes to 510(k) cleared medical devices. So this pilot is for sterilization providers with an Established Category B, or novel sterilization method, as described in FDA's 510(k) sterility guidance. It's intended to help with changes to a cleared medical device sterilization method from a fixed-chamber ethylene oxide sterilization cycle to whichever Category B or novel sterilization method is described in the master file.

Under the conditions that are outlined in the pilot notice, device manufacturers with devices that are in the scope of an accepted master file can reference the master file and include the related validation information in their internal documentation rather than submit a new 510(k) for that sterilization change. And to date, we've accepted one master file through this pilot program.

Finally, on April 11 of last year in 2023, we announced our Radiation Sterilization Master File Pilot Program. And again, this is for companies that sterilize single-use PMA approved devices using gamma

radiation or using ethylene oxide. It's open to all contract sterilization providers who might be able to implement the sterilization changes that are described within that pilot scope.

Again, it's a voluntary pilot. And it's intended to help contract sterilizers and device manufacturers make changes to sterilization methods or to advance some of their alternative ways to sterilize approved medical devices. This can include things like changing the radiation source, so from gamma to e-beam or x-ray, for example, in a least-burdensome regulatory approach. And to date, one master file has been accepted through this program.

Now, if you'd like more information regarding these pilot programs, I definitely encourage you to visit our web page, Sterilization for Medical Devices. And for detailed information about the pilot scope and procedures, please see the individual Federal Register notices for each pilot. These are included in the resources slide at the end of today's presentation. We also plan to talk more about these pilots with more granularity in a future town hall, so I definitely want to plug the future town halls. So please stay tuned.

Now I'll turn it over to my colleague Dr. Lisa Simone to talk about the next learning objective.

Lisa Simone: Thanks, Ryan. And now we'll share how FDA is considering what might be in the art of the possible for transitioning some devices from EtO to another sterilization modality. Although FDA has been actively involved in several areas, we wanted to catalyze efforts to meet some of the key 2019 recommendations.

To do so, we needed a cross-functional team to further advance innovation in sterilization methods to explore alternative modalities and to enhance our engagement with external stakeholders and with state and federal partners. We knew a nimble response required expertise in regulatory science, regulatory review, policy, supply chain, and incident response. And to meet those needs, we launched the EtO Tiger Team in early 2023 to integrate with existing CDRH efforts. Based on our initial stakeholder outreach and our own internal analysis, we realized the value of regular communications with you, so we launched this town hall series.

This slide illustrates the CDRH-wide participation on the EtO Tiger Team by office and functionality. The Office of Readiness and Response within the Office of Strategic Partnerships and Technology Innovation, or OST, brings expertise in incident response and standards and a deep involvement of engagement across government and external partners.

The Office of Supply Chain Resilience, also in OST, adds expertise in supply chain resiliency and shortage assessment. Our Office of Product Evaluation and Quality, or OPEQ, brings expertise in review practices, policy incentives, significant sterilization subject matter expertise, additional device shortage capabilities, and includes our focal point programs that Lieutenant Commander Steffen will mention later.

The Office of Science and Engineering Laboratories, or OSEL, provides expertise in sterilization and regulatory science, and our Office of Policy for policy and regulatory council needs, and finally, our Office of the Center Director for international outreach support and our communication strategy.

The Tiger Team initiated informal outreach to better understand the opportunities and the challenges that medical device manufacturers and sterilizers may be facing as you practically consider reducing EtO use and adopting alternative sterilization modalities. We asked about the use of EtO and other sterilants across medical device portfolios and approaches considered to reduce EtO use. We asked about challenges and successes using alternative modalities, including gaseous and radiation-based sterilants. We also gathered ideas for how FDA could help support expanding the use of alternative modalities or the use of more than one sterilization modality for a particular device.

FDA understands that many portfolios are still heavily reliant on EtO use, despite efforts to reduce EtO use or to transition to other sterilization modalities, such as Vaporized Hydrogen Peroxide, or VHP. And we hope you've seen our January 8 update to the 510(k) sterility guidance adding VHP as a Category A sterilant. FDA is aware that, as radiation is the second most common sterilization method, it may be a reasonable option for shifting away from EtO sterilization for some devices.

As we mentioned on our January 10 town hall, challenges shifting away from EtO use fall into several categories, including materials of construction, device and manufacture complexity and scale-up, and regulatory constraints, just to name a few. Material compatibility is a primary concern-- that is, understanding how device materials might be impacted with other sterilization modalities, as well as understanding what testing would be needed to confirm the device remains safe and effective.

We understand that performing new material compatibility testing on all the materials used for a device construction for multiple types of sterilization modalities could be arduous. And currently, few resources are available with actionable information about material compatibility. We understand that some devices might be more straightforward to transition from EtO, for example, metal or mostly metal devices.

And we also understand that some devices might not be candidates to transition from EtO at this time and that efforts are underway to reduce existing EtO use overall. One example is by exploring sustainable or reduced EtO cycles while continuing to meet the recommended sterility assurance levels, as in our innovation challenge 2 for reducing EtO emissions that Dr. Ortega mentioned previously.

There are logistical challenges in switching modalities, for example, device and manufacturing complexity, sterilant penetration, and scalability. Packaging might also create logistical issues with kitted devices or when using sterilants that are not compatible with cellulose, a common packaging material.

Regulatory challenges include the potential need to submit a large number of premarket submission for changes in sterilization information and that this may present extra challenges for companies with an international presence. In summary, plans to reduce reliance on EtO are varied across the device sector. And this transition translates into a multi-year endeavor with a variety of challenges that will require significant resources.

FDA can provide assistance by providing clarity to industry on understanding the current regulatory review practices and when a new submission may be necessary. FDA appreciates that validating a new sterilization modality is time and resource intensive and, as a cross-cutting issue, wants to assure that we are promoting consistency in review practices across OPEQ review offices.

FDA also wants to assure that we're applying least-burdensome principles and streamlining not only performance requests as appropriate, but also considering bundling submissions as appropriate, and further promoting the master file concepts that were discussed earlier. We'll be discussing premarket considerations, including the use of master files in premarket review, in the next few town halls.

We recognize the importance and value of timely review and, in some cases, expedited review. During our Jan 10 town hall, we spoke about the Bivona tracheostomy shortage and our part in facilitating sterilization of a device at a different facility. And we're considering ways that we can continue to be helpful in these types of scenarios.

As industry often operates in a global marketplace, we want to assure that we are embracing opportunities to coordinate with international agencies and recognize that potential flexibilities provided by one agency may inadvertently raise logistical issues with others. And FDA could also potentially provide input to technical discussions, for example, developing technical rationales for equivalency between various radiation modalities or providing education related to the biological indicator-bioburden validation approach and collaborating on data generation and standards to demonstrate that the performance of novel modalities is backed by independent literature and testing. FDA continues to explore how we might be innovative in reducing regulatory burden and furthering technical discussions so changes can occur quickly, like we did with the Master File Pilots.

Now I'll turn it over to Lieutenant Commander Scott Steffen to share other recent FDA activities and potential next steps.

LCDR Scott Steffen: Thank you, Lisa, and good afternoon, everyone. Our final topic today focuses on more recent and forward-looking opportunities the FDA and industry have taken, recognizing the fact that reducing reliance on EtO is a challenge larger than any of us individually and is best approached by working together.

As mentioned earlier, we want to keep our finger on the pulse of innovation. And your feedback helps us understand evolving challenges and successes. Looking at our innovation challenges alone, several manufacturers are exploring alternative EtO cycles and modalities. It's clear that collaboration and data sharing could be beneficial to industry, FDA, and the public in continuing the availability of safe and effective devices.

One collaborative opportunity is through the standards development process, which we will discuss in a future town hall. But I will note that FDA is currently involved in 40 standard development committees and working groups that develop, update, and revise sterilization-related standards. One such revision in process is for the Association for the Advancement of Medical Instrumentation, or AAMI, Technical Information Report-- TIR-- 17 for compatibility of materials subject to sterilization.

To include a larger data set of material compatibility, we acknowledge that material compatibility data is one rate limiter to facilitate meaningful movements away from EtO use. And this revision should allow a deeper understanding of information needed to assist in a change in sterilization modality.

Data sharing in the form of 506J notifications have been extremely beneficial in helping FDA prevent and mitigate medical device shortages. During the COVID-19 public health emergency, we worked closely with stakeholders to proactively assess supply chain problems and solve issues. And manufacturers are

encouraged to submit voluntary notifications using the links on this slide. In fact, FDA has received 506J notifications that indicate pressures and potential disruptions on the medical device supply chain resulting from sterilizer closures. Please note, the earlier FDA is made aware of a potential supply chain disruption, the more effective we can be in helping prevent and mitigate issues.

FDA also appreciates the value of broader collaborative activities, like we've observed in collaborative communities that bring together stakeholders to achieve common outcomes, solve shared challenges, and leverage collective opportunities. CDRH believes collaborative communities can contribute to improvements in areas affecting patients and health care in the United States.

We appreciate that a sterilization collaborative community may have value, given the challenges. And we look forward to any proposals from anyone interested in establishing such a new collaborative community. Please note that FDA does not initiate the formation of these collaborative communities. Rather, FDA may participate as a member. And resources are available on our website for anyone interested in establishing a collaborative community.

As Dr. Ortega mentioned, last year, we launched the Radiation Sterilization Master File Pilot to help firms using EtO or gamma to move towards x-ray and e-beam sterilization modalities. We also recognize the important roles standards play in supporting least-burdensome principles and facilitating exploration of alternative sterilization modalities.

Last July, FDA completely recognized ISO Standard 22441, which supports the use of low temperature vaporized hydrogen peroxide as an important alternative sterilization method. CDRH also recognized TIRs 17 and 104, intended to advance device sterilization methods and assist manufacturers making changes to radiation sterilization processes by addressing material compatibility and switching radiation sources.

Like Dr. Simone mentioned earlier, we recently updated our 510(k) sterility guidance based on the recognition of ISO 22441 to move vaporized hydrogen peroxide from an Established Category B to an Established Category A sterilization method, a modality we're aware industry has been actively exploring for several years.

This exemplifies our commitment of advancing sterilization innovations with long histories of safety and effectiveness and for reducing regulatory burden. FDA continues to participate in conferences and workshops to socialize our efforts, address misconceptions, and dialogue with you on important questions and addressing reliance on EtO.

The last bullet is not a recent action but is included to highlight the involvement of CDRH's sterility focal point program in supporting the Tiger Team and harmonizing sterilization-related review practices across OPEQ. The sterility focal point program has sterility focal points in each office, who serves as a resource for reviewers and provides input into our cross-cutting sterility activities to ensure they are as broadly applicable and useful as possible.

Before I wrap up for today, I'd like to summarize our progress on the 2019 advisory committee meeting recommendations as we look to the future. Industry suggested regulatory flexibility. And we shared that information on the three master file pilot programs as a starting point to address suggestions. We mentioned the recent recognition of Standards List 60 and encourage collaborative participants in

relevant standards development activities. In addition to reporting device shortages via 506J notifications mentioned earlier, we enhanced our ability to respond to device shortages by creating our Office of Supply Chain Resilience.

The last three recommendations speak to communication and collaboration across our broad stakeholder base. We continue to explore strategies and opportunities to reduce EtO use and a shift from EtO to other modalities. And we hope to discuss these more in a future town hall.

The next two slides serve as a resource list of the full URLs mentioned in this presentation.

In summary, we've shared a broad set of FDA activities and engagements from 2019 to the present, outlined the current challenges with EtO medical device sterilization, and some more recent efforts that both FDA and industry are doing in response. We also discussed our progress with respect to the 2019 advisory committee recommendations, the launch of the EtO Tiger Team to accelerate activities, and goals for continued collaboration.

Before we open up the discussion, I am excited to announce our next town hall on February 7, where we plan to discuss premarket submission expectations for sterilization-related submissions. Information about the town hall series can be found using the link here.

That concludes our presentation portion of the town hall. So let me pass it to Joe Tarta to move us into our Q&A session.

Joseph Tartal: Thank you, Scott, Lisa, and Ryan and Aftin for your presentations. We'll now transition to our interactive comments and questions and answer segment.

Joining our presenters today as part of this segment, we have Dr. Suzanne Schwartz, Director of the Office of Strategic Partnerships and Technology Innovation, or OST, and Dr. Tammy Beckham, Director of the Office of Supply Chain Resilience in OST. Thank you both for joining our panel today.

Before we begin, I'd like to go over how we'll manage this segment. 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. When prompted, please select the blue button to unmute your line. Identify yourself and your organization and then engage with our panelists with your question or 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 your comment, please lower your hand. If you have another question or comment, please raise your hand again to get back into the queue. Then I'll call on you as time permits.

Now, as we wait to interact with you today, I'd like to circle back to our presenters and panelists with a few questions. So the first question I have is for Lisa. You shared that FDA continues to receive information about current sterilization challenges. Is there any additional information that might be helpful?

Lisa Simone: Yes, Joe, thank you. We welcome your thoughts on several topics during today's Q&A session or via our mailbox that you see on the screen. 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.

But here's the information that we're interested to get-- updates on anything that you have related to opportunities to reduce EtO use and/or switch to other sterilization methods. And I'll give you a few examples to think about. One, what are your approaches or success stories for switching modalities, for example, EtO to radiation, or for reducing EtO use, like reducing or optimizing existing cycles or developing new cycles? And what information was vital to support your decision-making?

Two, what are the major challenges or showstopper issues switching modalities or reducing EtO use and why? And third, if you could suggest one sterilization-related action for FDA to consider, what would that be? Back to you, Joe.

Joseph Tartal: OK, thank you, Lisa, and thank you for that very helpful additional information that's being looked for. Our next question is for Tammy. What do you do with 506J shortage information that you receive?

Tammy Beckham: Hi. Thanks, Joe. Thanks for that question. So FDA utilizes the information that's provided through 506J notifications to conduct impact assessments so that we can understand the potential patient impact and supply chain impacts of a disruption and/or pending shortage. These impact assessments are utilized then to inform implementation of both regulatory and non-regulatory mitigations. So just to give you an idea of what some of those are, obviously, the FDA can use this information to inform whether or not we would use regulatory discretion, conduct letters to health care providers, expedite 510(k)s, et cetera. So those are examples of regulatory mitigations.

And the FDA also works across the government with the Administration for Strategic Preparedness and Response, the Department of Transportation and Commerce and others to inform different types of mitigations that are nonregulatory. So those include prioritization of raw materials and components for medical devices when the supply chain disruptions occur, or prioritization of transportation.

As an example, though FDA doesn't have delegated authorities under the Defense Production Act, we have worked with ASPR and the Department of Commerce to inform the use of DPA priority ratings and priority request letters during the COVID public health emergency. So these are just a few examples of how we use this information, largely to conduct these impact assessments, which then we rely on and other federal partners rely on to implement those mitigations. Back over to you, Joe.

Joseph Tartal: OK, thank you, Tammy, for that very comprehensive answer on the information for 506J shortages. Our next question is for Suzanne. Are there any efforts to reach consensus or streamline requirements across the international community?

Suzanne Schwartz: Yeah, thanks, Joe. So let me give a high-level response to that, knowing that we will be, in the future, taking deeper dives specifically around the standards-related question. So one of the ways that CDRH engages internationally is through the voluntary consensus standards process.

Specifically, CDRH helps to drive development, as well as recognition and appropriate use of internationally accepted medical device sterilization consensus standards. But we also attend global conferences, we engage with other jurisdictions, so that we can better understand the challenges, as well as the opportunities, for harmonization of medical device sterilization. Back to you, Joe. Thank you.

Joseph Tartal: Thank you, Suzanne. Now we will now hear from our first live audience member. So Liz Claverie, I'm unmuting you. Please unmute yourself and ask your question.

Liz Claverie: Hi, thank you all very much. Good afternoon, FDA, and thank you, as always, for having these very important town hall meetings. It is really appreciated. My question for today is, if you have manufacturers that are working towards moving their devices from traditional ethylene oxide to some other terminal sterilization method, and they have technical questions, what's FDA's recommended mechanism that a sponsor should utilize in order to seek assistance? Is it something like a Pre-Submission? Is it applying to the FDA STeP program, or et cetera? And thank you very much.

Joseph Tartal: OK, thank you, Liz. Ryan, would you like to respond?

Ryan Ortega: Yeah, thank you. That's a really good question. And I'd like to provide some feedback about some actions that you could take. In my mind, the first step if you've got specific questions of a technical nature about a change to sterilization or some component of a future regulatory submission-- I found that our Pre-Submission process, which is a submission type under our Q-Submission Program-- it has been a very effective way of getting-- for FDA providing feedback to those sort of specific questions.

We do have a specific guidance that talks about the Pre-Submission process, the expectations for what can go into a Pre-Submission, how to ask the best questions, how to make the most effective use of those sort of meetings. It has been my experience that that is an excellent venue for asking specific questions on a subject matter area like sterility and getting feedback from the device team who is going to be regulating your specific device. So I would definitely recommend the Pre-Sub process for those sort of questions.

Joseph Tartal: OK, thank you for that response. Our next question comes from Katahar Kahala. I'm unmuting you. Please unmute yourself and ask your question. Are you there? Katahar, please unmute yourself and ask your question.

OK, with that, we'll go on to our next question. Byron Lambert, I'm unmuting your faction. Please unmute yourself and ask your question. Byron Lambert.

Byron Lambert: Thank you very much, Byron Lambert from Abbott. It's difficult to express how grateful the industry is for the FDA's leadership and seeking the best for patients in terms of, again, just getting momentum within a large multinational company within the standards arena, as you mentioned, Working Group 96 and additional new work item proposals going, and in socializing with other regulatory bodies. It's just enormous. So thank you for the summary today and for what you're doing for the patients in the industry.

The question relates to the new guidance that was just updated in January. Thank you again for that and for your timely leadership to recognize VHP. The question relates to the novel methods, and does the FDA have a plan to update guidance on a regular basis? It seems like it'd be appropriate to review those

list of novel ones and update it. And then the question would be, what additional information would you need on modalities, like nitrogen dioxide or chlorine dioxide, to add those to the list of novel modalities?

Joseph Tartal: OK, thank you for your question, Byron. Ryan, would you like to take this?

Ryan Ortega: Sure, I'll take a stab. Yeah, appreciate the feedback that we've been receiving and the interest that we've been receiving and the updated 510(k) sterility guidance. So some initial thoughts with respect to update strategy and the novel category specifically. While we don't generally discuss publicly our future plans for updating guidance, I will say that, generally, we do try to regularly assess, Is this guidance still relevant? Does it need specific targeted updates? Does it need broader updates? In fact, our recent update to that 510(k) sterility guidance came out of just such a internal consideration and taking a look at where that guidance sat after that standards recognition.

So with respect to the novel sterilization methods, I definitely want to flag that the list that we have in the guidance-- it provides some examples, but it's certainly not exhaustive. We know that there's a lot of innovation going on and that there are groups across the country, or really across the world, who are working on developing new alternative methods, working on improving what's out there, and coming up with new ideas.

So that said, if you do have feedback for the guidance, or if you have things that we should consider, there are a couple of ways to share that feedback. One, there is contact information in the guidance. That lists some ways to reach out to us to provide questions, information, feedback, that sort of thing. But there's also the public docket that is open for all our guidances and can be commented on at any time.

If you do have specific feedback for changes to the guidance or things that you would like to see added or thoughts about policies or procedures described in our 510(k) sterility guidance, would definitely encourage you to submit those that way so that we can take a look and consider them. I hope this was helpful for providing some insight into how all guidances, but really that particular guidance, got updated and gets updated in the future.

Joseph Tartal: OK, thank you, Ryan, for that information. Our next question is from Marvin C. Brown IV. Marvin, I'm unmuting you please-- oh, he just dropped off. Pardon. Let's try this. OK, I'm unmuting you. Please state where you're from and ask your question.

Marvin C. Brown IV: Thank you so much. My name is Marvin Brown. I'm an attorney at Earthjustice. I just wanted to ask, now that hydrogen peroxide has been moved up into a category A sterilization method, I was just wondering if FDA has any estimates of how many of the current products-- I believe it estimates that 50% of current medical devices are sterilized with ethylene oxide. How many of those devices does the FDA estimate can be shifted over to hydrogen peroxide as a sterilization modality?

Joseph Tartal: Aftin, would you like to respond?

Aftin Ross: Yes, thank you. So I think that this is a challenging response for us to give because some of this is going to be dependent on some product-specific characteristics, certainly the materials that the product is made of. But also how they are combined certainly will also play a role with regard to a device's ability to go to VHP.

One of the other considerations that you also have related to VHP related to compatibility is that it is not compatible with cellulosic materials, so with cardboard. And so that also necessitates, then, a shift in how products are sterilized. It's likely that you would need to move more to an inline sterilization method. And that brings with it a different additional infrastructure and other challenges.

So while we have from some of the different standards and things that are out there, some insights into where there might be some material compatibilities, and certainly what you need to do to validate, you often don't know until you actually start that validation process whether or not you might be successful. And then even if you can, from a material compatibility perspective, potentially shift product, that there's a longer road to actually determining how you would do that from an infrastructure perspective because you're not typically going to be able to leverage contract sterilization options, as I was saying, because a lot of that's going to likely have to move to being inline in that production facility.

So that's kind of how I would respond to that. Do note, I mentioned the fact that there are some standards that help with material compatibility, but didn't say which one. And so I want to make sure that it's known that it's the TR17 that has some information with regard to VHP compatibility as well.

Joseph Tartal: OK, thank you, Aftin. Our next question is from Maruti Sinha. Maruti, I'm going to give you permission to ask your question. Please unmute yourself, note where you're from, and ask your question.

Maruti Sinha: Sure, thank you. My name is Maruti Sinha. I'm from Medtronic. I have a question on your point, risk-based SAL level for some medical devices, right? I need some clarity on what those medical devices you are talking about. Does it include implantables?

Joseph Tartal: Ryan, would you mind taking this?

Ryan Ortega: Yeah, definitely. Again, this is an important question because that's potentially one tool in our toolbox for reducing ethylene oxide use. I will say that I don't know that we got specific recommendations from the advisory committee on that topic as granular as saying specific devices. You know, I think taking a risk-based approach to sterilization that is device specific, just as by its very nature, will rely on some assessment, some knowledge, of device-specific characteristics, like intended use, the configuration of the device, the materials, all of that.

So while we don't have a specific device or a device type in mind, I will note that we do have a few FDA-recognized standards about alternative SALs. And we have in some of our guidances indicated that, potentially for some skin-contacting-only devices-- so those devices that only contact intact skin and don't, for example, contact broken skin or mucosal membranes-- alternative SALs may-- again, may-- be appropriate.

Ultimately, though, if a device manufacturer is considering a risk-based assessment to support an alternative SAL, I strongly encourage you to go to your specific review division to discuss that idea because the considerations can become quite device specific.

Joseph Tartal: OK, thank you, Ryan, for that answer. Our next question is from Nagru Beluh Mabasa. I'm unmuting you. Please note where you're from and ask your question.

Nagru, are you there? OK, we'll go to our next question. Leila Ramani.

Beluh Mabasa: Yes, yes, please.

Joseph Tartal: Oh, hold on.

Beluh Mabasa: Please.

Joseph Tartal: OK, go ahead.

Beluh Mabasa: Yes. OK, thank you very much for the time. My name is Beluh I am from Indonesia. I have a little bit question please. Just a minute.

Has International Medical Regulation Forum published any guidance related to this case? And to what extent is the FDA collaborating with the International Medical Regulation Forum until right now, especially for the recognized standards that they have published by the Food and Drug Administration? Thank you very much for the time. Hello?

Aftin Ross: Good afternoon. Nope, sorry. This is Aftin. Good afternoon. No, so certainly, I think you're mentioning IMDRF. And as many people might know, FDA is actually the co-chair for IMDRF this year and has been actively engaged since its inception. Certainly, as part of how we think about international complex challenges, we want to be engaging with our international partners on these types of topics. I'm not aware of a specific IMDRF item that is related to this right now. But I know there are some more general items that are being worked on that might also have some applicability just in general kind of regulatory program and guidance. But that's certainly something that could be considered in the future.

Joseph Tartal: OK, thank you for that response. Our next question, I'm going to Khatereh Calleja. I'm unmuting you. Please unmute yourself and ask your question.

Khatereh Calleja: Can you hear me this time? [LAUGHS]

Joseph Tartal: Yes, I can, loud and clear.

Khatereh Calleja: Excellent. Thank you very much. And it's Khatereh Calleja. Thank you very much with that, a challenging name. On behalf of the industry, I just wanted to personally thank the Agency for your ingenuity and partnership work with the innovation challenges, the collaboration on the master pilots. They've been incredibly helpful to support optimization efforts and, importantly, patient access to critical medical devices. This work is so important for the delivery of life-saving technologies for many health care providers and the patients we serve.

So with that in mind, my question was, you had spoken, the team, about reducing paper instructions, such as electronic IFUs from devices being sterilized as part of efforts where possible, support optimization. This is something the industry has long supported and moving to electronic IFUs as part of today's modern age and also just the way that folks communicate and as an important way in terms of an opportunity in sterilization. Can you speak to FDA's thinking on reducing paper instructions for devices in the space and some opportunities for collaboration? Thank you.

Joseph Tartal: OK, thank you for your question. Lisa, would you like to respond?

Lisa Simone: Sure, yes, yes. So the paper and e-labeling discussion has something that-- it's been something that's been raised for several years. It was brought up during the advisory committee meeting in 2019. And I know that there's been several discussions since then. We have received some comments over our outreach on the last year for folks who are interested in additional information about potential e-labeling. And over the course of the COVID public health emergency, there were some flexibilities related to such as a part of that event.

So we do have some internal discussions trying to explore how that might be possible. At this point in time, there are some advances in some areas with devices from the public health emergency that may or may not be the best starting avenue for e-labeling at this time. We are looking to find a device area or a particular situation that could make an impactful change in the amount of ethylene oxide that's used, so something that could be a disposable high-volume device. And we're focusing some of those efforts in that area.

So I would say, for that, continue to stay tuned. I think that there may be some additional outreach and questions in that area. If you do have some specific thoughts about devices where this might give us the so-called best bang for the buck, then we'd certainly be interested in your input. Thanks for that really great question, Khatereh.

Joseph Tartal: OK, thank you, Khatereh. We have time for one last question. Leila Roumani, I'm unmuting you. Please unmute yourself and ask your question.

Leila Roumani: Hi, can you speak to differences, if any, in the 510(k) submission process for reprocessing single-use medical device components for POC versus OTC?

Joseph Tartal: Ryan, would you like to answer this one?

Ryan Ortega: Can I just get some clarification. Is this about medical device reprocessing?

Leila Roumani: Yes.

Ryan Ortega: Yeah, appreciate that clarification. So today, we're really only talking about terminal sterilization of single-use devices rather than reprocessing topics. But what I will do is direct you to our reprocessing guidance for additional information on reprocessing, and also for potential contact information for that guidance. There may also be some helpful guidance on our Device Advice website that's run by our Division of Industry and Consumer Education too.

Joseph Tartal: OK, thank you, Leila. That will wrap up our comments and questions and answer segment for today's town hall. Thank you all for your participation today. I'd now like to turn it back over to Aftin to provide today's final thoughts.

Aftin Ross: Thank you again for coming to the town hall today. We again appreciated the robust discussion that we had during the Q&A, starting to be later in the day on the Friday afternoon. It was

very interactive, and we heard about a variety of topics, such as international harmonization, alternative sterilization modalities, as well as risk-based sterility assurance, in addition to e-labeling.

We are very much committed to continuing the dialogue on these critical medical device sterilization topics to try to make sure that patients and providers have the medical devices that they need. Thanks again for coming, and we hope you have a wonderful weekend.

Joseph Tartal: Thanks, Aftin, for those final thoughts. As was mentioned earlier, the slides for today's presentation are currently available on CDRH Learn at the link. Go to this slide. Go to CDRH Learn, section Specialty Technical Topics, subsection Sterility. A recording of today's town hall and transcript will be posted to CDRH Learn here within the next couple of weeks. Here's also a screenshot of where you can find these materials.

As mentioned earlier, if you have additional questions or comment about today's topic or presentation or thoughts for future town hall, please email us at MedicalDeviceSterilization@fda.hhs.gov. If you have any general questions about today's town hall or general medical device questions at all, feel free to reach out to DICE@fda.hhs.gov.

Finally, looking ahead, please join us for the next Medical Device Sterilization Town Hall. That will be town hall number 3, scheduled for Wednesday, February 7, from 3:00 to 4:00 PM Eastern time. For a listing of all upcoming town halls and webinars, please visit our CDRH Webinar page found at the link at the bottom of the slide.

This concludes today's town hall. Thank you all again for joining us.

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