Medical Device Sterilization Town Hall: Sterilization Short Topics, Series Impact, Wrap Up, and Next Steps
December 4, 2024

Moderator: CDR Kim Piermatteo

CDR Kim Piermatteo: Hello, everyone. Thanks for joining us for our 15th and final Medical Device Sterilization Town Hall for 2024. 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 within FDA's Center for Devices and Radiological Health. I'll be serving as a moderator for today's town hall.

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 multipronged approach, including regulatory flexibilities, supply chain analysis and mitigation, collaboration, innovation, and communication, including this series of town halls.

For today's town hall, we'll begin with a few opening remarks, and then we'll discuss two short topics, the first being the final guidance titled "Transitional Enforcement Policy for Ethylene Oxide Sterilization Facility Changes for Class III Devices." And then the second topic will be Research and Modeling on Diffusion of Vaporized Hydrogen Peroxide Through Select Polymeric Materials. Then we will discuss the impact of this town hall series as well as wrap up this series and explore next steps.

I'd now like to share a few administrative items before I introduce and turn it over to our panelists. First, please make sure you've joined us through the Zoom app and not through a web browser to avoid technical issues, and second, 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.

For today's town hall, we have many people from CDRH here, and I'm excited to introduce all of them to you. First is Dr. Suzanne Schwartz, Director of CDRH's Office of Strategic Partnerships and Technology Innovation, or OST; Dr. Lisa Simone, Senior Health Scientist and EtO Incident Lead within the Office of Readiness and Response within OST; Dr. Ryan Ortega, Regulatory Advisor on the Regulatory Policy and Combination Products Staff within CDRH's Office of Product Evaluation and Quality, or OPEQ; Dr. Jon Weeks, Assistant Director in the Division of Biology, Chemistry, and Materials Science within CDRH's Office of Science and Engineering Laboratories, or OSEL; Commander Tamara Rosbury, Health Scientist and EtO Incident Response Team Member within the Office of Readiness and Response within OST.

Also joining us today is Bella Pelina, Policy Analyst on the Clinical and Scientific Policy Staff in OPEQ; Jennifer Berg, Senior Staff Fellow in the Office of Health Technology Number 4 in OPEQ; Jhumur Banik, Team Lead and Biomedical Engineer in the Office of Regulatory Programs in OPEQ; Dr. David Saylor, Research Materials Engineer in the Division of Biology, Chemistry, and Materials Science in OSEL; Dr. Bonnie Liu, Research Scientist in the Division of Biology, Chemistry, and Materials Science in OSEL as well.

And then also joining us is Commander Scott Steffen, Senior Program Management Officer and EtO Incident Lead in the Office of Readiness and Response within OST; Christopher Dugard, Assistant

Director in the Office of Health Technology Number 4 in OPEQ; Dr. Tammy Beckham, Director for the Office of Supply Chain Resilience in OST; and Dr. Aftin Ross, Deputy Director for the Office of Readiness and Response within OST.

Thank you all for joining us for our town hall today. I'd now like to turn it over to Suzanne to get us started.

Suzanne Schwartz: Alright, thanks so much, Kim. Hello, everyone. I know I speak on behalf of the entire team at FDA's Center for Devices and Radiological Health in expressing our appreciation and our deepest gratitude for your staunch support of the Medical Device Sterilization Town Hall series over the course of this entire year.

Delivery of healthcare across our nation depends upon the ready availability of safely sterilized medical devices. The resilience of our U.S. healthcare and public health critical infrastructure is therefore, by extension, predicated upon ready availability of safely and effectively sterilized medical devices. This series discussed the current medical device sterilization landscape and potential activities to advance innovation in the field of medical device sterilization.

Stated most simply, our objective in launching these town halls was to engage directly with you to provide an interactive means for sharing information, asking questions, and providing comments. Ultimately, this type of whole-of-community approach serves to strengthen our collective efforts and builds upon FDA's tireless commitment to protect and promote public health.

Now, as you know, this is not a finished story. Medical device sterilization continues to evolve. In 2024 alone, FDA has issued several sterilization guidances, the most recent one issued on November 25, and we will, in fact, be discussing that one today. Also, EPA released updated requirements for ethylene oxide sterilization.

As the sterilization landscape evolves, FDA evolves with it to ensure that patients and providers have timely and continued access to safe, effective, and high-quality medical devices. The 15 town halls that we've had over the course of this year highlight the many efforts FDA has undertaken as part of a multipronged, forward-leaning approach to evolve and innovate in the interests of patient safety, and I can assure you that our work here continues.

Just to put a finer point on it, at FDA, we found that to identify solutions to complex challenges, we need to actively engage a wide range of stakeholders with diverse perspectives. The town hall series, we believe, has been a highly effective way of doing that. These sessions have served as a catalyst for information sharing and stakeholder collaboration across the ecosystem.

I'll wrap up these remarks by further underscoring my main takeaway here, and that is medical device sterilization benefits from a whole-of-community approach, period, full stop. It enables acceleration of individual efforts, whether that be new methods, streamlined processes, or a greater understanding of material compatibility.

Your collective inputs inform our understanding of what's in the art of the possible. As the series concludes, please know that FDA remains dedicated to its collaborative approach for advancing medical

device sterilization so that patients and providers have access to the devices they need. And with that, I thank you so much again for your attention, and we'll turn the program over to Dr. Lisa Simone.

Lisa Simone: Thank you, Suzanne, for setting the stage, and thanks to everyone for joining us today for our 15th Sterilization Town Hall. It's been a real pleasure coming to you every few weeks throughout this year, sharing our activities and hearing from you directly. This series has been well informed by your thoughtful comments and questions and suggestions, which actually started arriving the day after our very first event in January.

Our final town hall today has a full agenda, and even though it's quite busy, I'm excited that the content spans a range of activities, from collaborative research to new transitional enforcement policy. I hope you'll come away from today's event with a greater awareness of the broad activities where FDA can contribute and that you'll explore some of the series content that you may have missed.

By now, I think everyone is familiar with this slide and how it grows with our activities as they progress. Today, we're highlighting the new guidance for topic one and town hall launches for topic three. Our panelists will mention nearly every item on this timeline as we share how the town hall series enabled us to have conversations with you about this wide range of activities.

Today, we have three discussion topics. We'll start with some late-breaking news, which is the publication last week of the new “Transitional Enforcement Policy for Ethylene Oxide Sterilization Facility Changes for Class III Devices" guidance. Our panelists will also provide a brief comparison to the existing PDA/HDE enforcement policies.

Our second topic is a bit different from previous town hall topics. Our Office of Science and Engineering Laboratories accelerates access to innovative, safe, and effective medical devices through best-in-the-world regulatory science. One approach our scientists and engineers take is through collaborative activities that Suzanne mentioned with a broad range of interested partners. And today, our OSEL panelists will share some collaborative research and modeling on the diffusion of vaporized hydrogen peroxide, or VH2O2, through select polymeric materials and discuss potential impacts.

Lastly, as this is our final planned event, our panelists will discuss the scope and impact of the town hall series and related FDA activities and explore potential next steps in the continued effort to reduce reliance on ethylene oxide for sterilization of medical devices.

And now I'd like to turn it over to Ryan for our first discussion for our first topic today, the new guidance.

Ryan Ortega: Yeah, thanks, Lisa. I'm definitely excited to start off with this really important topic. As you mentioned, we recently published a guidance document entitled "Transitional Enforcement Policy for Ethylene Oxide Sterilization Facility Changes for Class III Devices" on November 26 this year.

You may also hear us refer to it as the ethylene oxide site change guidance or something similar. The group of people that you see on the screen right now will answer a few questions about the guidance, and I'd like to start our conversation about the guidance with Bella. Bella, can you tell us a little bit about why we developed this guidance?

Bella Pelina: I'd be happy to, Ryan. I'll be starting off with some contexts. FDA plays a critical role in helping prevent and mitigate potential medical product impacts, and as part of this work, we closely monitor the supply chain effects of temporary or permanent closures and potential closures or capacity reductions of sterilization facilities that use EtO gas to sterilize medical devices prior to their use.

This helps prevent and minimize impacts to patients who need access to these important sterile devices. FDA developed this guidance to provide an enforcement discretion policy to respond to anticipated changes in EtO sterilization activities as facilities work to advance orderly implementation of and compliance with EPA's rule. Additionally, this guidance was developed to prevent or mitigate the potential risk of supply chain disruptions or medical device shortages during the time period in which these manufacturers are transitioning to compliance with new requirements.

Ryan Ortega: So thanks for providing that information, Bella. You mentioned new requirements that sterilizers would have to meet. This would be the final rule published by the Environmental Protection Agency, which amended its National Emission Standards for Hazardous Air Pollutants, or NESHAP, right?

Bella Pelina: Yes, that's right.

Ryan Ortega: And so for everyone's edification listening, EPA's amendment of the NESHAP revised their existing standards and established new standards for ethylene oxide emissions. EPA also conducted a registration review of ethylene oxide, and they issued a proposed interim decision in April of 23. I imagine that this will mean that some ethylene oxide sterilization facilities will be making changes in order to comply with the new requirements, right?

Bella Pelina: For sure. FDA anticipates that some EtO sterilization facilities will need to install controls or make changes to their operations as they prepare to comply with these actions. This means that some facilities may either temporarily reduce their sterilization operations or make shifts in the location of their sterilization operation during this time of transition.

Something I think that's worth mentioning is that some companies involved in medical device sterilization have installed or are already planning to install emissions controls to comply with EPA's final rule and to anticipate steps that they might take related to EPA's registration review, which is really great.

Ryan Ortega: So Bella, let's get into the meat of the guidance a little bit. What exactly is the enforcement policy that's being introduced via the new guidance?

Bella Pelina: That's an important question, isn't it, Ryan? As many of those attending today may be aware, for devices subject to premarket application, PMA, or humanitarian device exemption, HDE, requirements, submission of a 180-day PMA site change supplement or a 75-day HDE site change supplement is required prior to use of a different manufacturing site that affects the device's safety or effectiveness.

However, to prevent and mitigate potential concerns with medical device availability that may result from changes in sterilization operations, during the time period in which manufacturers are transitioning to compliance with these new requirements, FDA is seeking to facilitate sterilization site changes more quickly to help prevent and minimize potential supply interruptions.

The enforcement policy outlines the general framework wherein FDA will determine on a case-by-case basis whether the exercise of enforcement discretion related to the sterilization of Class III devices at a proposed new sterilization location and subsequent distribution of such devices prior to approval of a PMA or HDE site change supplement is appropriate.

Ryan Ortega: Yeah, thank you for describing the enforcement policy, Bella. Now, can you give us a bit of an overview of the framework that we'll use to determine whether or not enforcement discretion is appropriate?

Bella Pelina: Sure, Ryan. Device manufacturers who wish to have FDA consider the exercise of enforcement discretion related to the implementation of a sterilization site change and subsequent distribution of sterile devices are recommended to submit an informal notification as recommended in section 5 of the guidance. Following receipt of this informal notification, FDA will evaluate the information and then issue correspondence to the PMA or HDE holder with its determination of whether enforcement discretion is appropriate in a given case.

Ryan Ortega: So then once we complete our evaluation of the information that we get for a specific case, what happens if we determine that enforcement discretion is appropriate?

Bella Pelina: Where enforcement discretion is determined to be appropriate, FDA does not intend to object to a device manufacturer beginning sterilization of the subject device at the proposed alternate sterilization facility prior to approval of the required PMA or HDE site change supplement.

Once the correspondence is issued to the PMA or HDE holder that enforcement discretion is appropriate for their specific case, then the device manufacturer should begin preparing a PMA 180-day site change supplement or an HDE 75-day site change supplement for submission to the FDA within 120 calendar days from the date on the correspondence.

Ryan Ortega: So then in the opposite case, what happens if FDA indicates that the exercise of enforcement discretion related to implementing a new alternate sterilization facility is not appropriate?

Bella Pelina: Ah, you're asking the tough questions, Ryan. If enforcement discretion is determined to not be appropriate, then a PMA or HDE holder may still submit a site change supplement, but it's going to be reviewed according to the normal timeline for that type of supplement.

Ryan Ortega: Yeah, thanks, Bella. So it sounds timely notification is going to enable us to work proactively with all of the interested parties to develop a plan to mitigate potential impacts on the sterile device supply chain and, most importantly, to mitigate potential negative effects on patient care, which, again, is so critical.

Jennifer, I think I want to turn to you. Are there any recommendations about the type of information that manufacturers should include in their notification?

Jennifer Berg: Sure, Ryan. I'd be happy to discuss some of those points. The information that FDA recommends for inclusion in the notification is outlined under Section 5(c) of the guidance. I'm not going to go over each item but wanted to really highlight the sterilization related information that FDA

recommends that manufacturers include in their notification. This information includes the following five points and enables FDA to appropriately identify the specific sterilization sites that are affected and evaluate any potential impacts of the notification.

The first is the name, address, and FDA establishment identification for the current and proposed new or any additional sterilization sites. The second would be identification of whether the proposed sterilization site or sites were previously cleared under the original PMA or HDE or a PMA or HDE supplement. Number three is identification of whether current and proposed alternate or additional sterilization sites are ready for FDA inspection, if applicable. Number four is the date in which the site change will be implemented. And number five is a brief summary of any changes to the sterilization process that may result from the site change. This includes a description of any changes in sterilization equipment, such as a manufacturer, model, chamber size, and this information could be provided in a set of statements or even in a tabular format.

The FDA also recommends that the notification include a statement of affirmation signed by a responsible person of the firm required to submit the premarket approval supplement. This information will help FDA identify whether the proposed sterilization site change is within the scope of the policy described in the guidance.

Ryan Ortega: Thanks, Jennifer. That's all really helpful. That statement of affirmation you mentioned, what exactly is that telling us?

Jennifer Berg: Thanks, Ryan. Yeah, I'd be happy to provide a few more details on that. The signed statement affirms that the notification pertains to a Class III device and is also not considered a combination product. It also affirms that no changes have been made to the device's indications for use, labeling or packaging, and also affirms that no changes to facilities or establishments use for manufacturing, processing, or packaging of the device outside of the sterilization. And it affirms that there are no changes to performance or design specifications, circuits, components, ingredients, principles of operation, or physical layout of the device. Also that there are no changes to the expiration date based on data obtained under a new or revised stability or sterility protocol that has not been approved by the FDA and affirms that there are no other changes that affect the safety or effectiveness of the device.

And lastly, it affirms that no changes have been made to the sterilization process apart from the sterilization facility and those changes necessary to facilitate a change in location, such as there's no changes to a different sterilant used, release criteria for this cycle, a sterility assurance level, and no major changes to the critical sterilization process parameters.

Ryan Ortega: Yeah, thank you, Jennifer and Bella both, for that really informative discussion on the ethylene oxide site change guidance. I also want to acknowledge that we have other PMA and HDE enforcement policies that we've published in other guidance documents.

So now, to help us delineate between them, Jhumur, I want to turn to you. How is this policy different from other PMA or HDE enforcement policies that we have in other guidance documents?

Jhumur Banik: Thanks, Ryan, and that's correct. There are other PMA or HDE enforcement policies that FDA has published, particularly one published in the guidance titled "Enforcement Policy for Certain

Supplements for Approved PMA or HDE Submissions." This particular guidance is intended to help address current manufacturing limitations, potential shortages or supply chain challenges that may be alleviated or mitigated by adding production lines or manufacturing at alternative sites.

Ryan Ortega: So like the ethylene oxide site change guidance, the new one, it sounds like the guidance you mentioned also deals with mitigating potential shortages and supply chain interruption. How is the scope of the guidance that you mentioned distinct from the new guidance?

Jhumur Banik: Yeah, so for the scope of this guidance that I mentioned, it covers limited modifications made to a device approved through the PMA program that triggers the requirement that a manufacturer submit a PMA supplement or a 30-day notice to the FDA.

It also applies to limited modifications that are made to a device approved through the HDE program that require manufacturers submit an HDE supplement or 30-day notice. So for example, the policy and the guidance considers modifications made to address component or material shortages, changes made to accommodate social distancing based on local conditions, changes in manufacturing facility or establishment, and changes to packaging procedures.

Ryan Ortega: Yeah, thanks, Jhumur, and real quick, what falls outside the scope of that guidance?

Jhumur Banik: So this guidance is not intended to address preventative measures that a sponsor is taking for a possible shortage in the future and also changes to the sterilization method that are generally outside the scope of this guidance. I do want to note that the following statement is included in this guidance, which states, "The policy set forth in this guidance does not apply to design or manufacturing changes made for reasons other than addressing manufacturing limitations or supply chain challenges."

Ryan Ortega: Yeah, thank you, Jhumur, and thank you also, Bella and Jennifer, for that very informative and interesting discussion. As a final note, I do want to flag for our audience that this new guidance does not supersede our guidance "Manufacturing Site Change Supplements-- Content and Submission" either.

I'd definitely encourage general device manufacturers and contract sterilizers to familiarize yourself with this new guidance and other guidances that have relevant information on sterilization and sterilization changes as industry works to ensure compliance with all the rules and regulations related to sterilization.

That concludes this particular topic, and so now I'll pass it over to Jon to get the discussion started on our next one.

Jon Weeks: Thank you, Ryan. We will now discuss our research efforts of modeling vaporized hydrogen peroxide, or VH2O2, penetration through medical device materials. CDRH supports collaborations between CDRH researchers and other scientists through tools such as research collaboration agreements. We engage with various entities, and the work we are sharing here today is the result of an RCA between FDA CDRH researchers and Medtronic scientists.

In the interest of time, we'll be only presenting this information at a high level, and we invite you to learn more in separate publications. Thank you to Medtronic for providing written approval for their name and our collaborative work to be presented here.

Dave, can you share with us the motivation and need for this collaboration?

David Saylor: Sure, Jon. I think we're all aware that the sterilization landscape is changing and there's a heightened need for alternatives to ethylene oxide and therefore for the adoption of gas or vapor phase sterilants that may be currently underutilized. Moreover, computational modeling approaches are somewhat routinely utilized to support radiation-based sterilization, but these types of approaches have not been widely leveraged to support gas or vapor phase modalities.

And so we think the development of these types of modeling approaches could facilitate adoption of EtO alternatives, and an example of this are devices like cardiac or neurological leads that currently rely on ethylene oxide permeation through device materials to sterilize interior surfaces that may ultimately come into either direct or indirect contact with patients. And the challenge is really providing empirical evidence that any alternative would exhibit not only sufficient permeation but also microbial inactivation properties at these interior surfaces.

Jon Weeks: Thanks, Dave. Now we will discuss our approach towards modeling permeation and then activation. Bonnie and Dave, can you share the approach on how we moved this forward?

Bonnie Liu: Sure, John. So the goal of this effort is to develop a physics-based computational model that can be used to predict the VH2O2 permeation through medical device polymers. There are challenges on the way to achieve our goal, so now I'm turning to Dave to talk about those challenges and our solutions to address them.

David Saylor: Thanks, Bonnie. Yeah, I think the biggest challenge with the development of any computational model is really having sufficient data to not only calibrate the model-- and what I mean by that is establishing material-specific parameters-- but then also to have independent data that can be used for validation of the model.

And a primary example of this is at the FDA, we don't have access to commercial sterilizers, so we're not really able to generate validation data that would be reflective of real-world use. And our solution to this was to establish a research collaboration agreement, or RCA, with Medtronic corporate research and development that Jon described up front that will help us address this challenge.

Jon Weeks: And just as a disclaimer before we continue, the findings and conclusions reported herein have not been formally disseminated by the U.S. Food and Drug Administration and should not be construed to represent any agency determination or policy. Dave, could you give us a high-level overview of how a physics-based model for VH2O2 sterilization might work?

David Saylor: Sure. So essentially, the model would map the concentration of VH2O2 that's applied within the chamber to the concentration that's actually delivered to interior surfaces of an enclosed medical device component. And the example we're showing here on the screen is the concentration profile within a chamber that contained a completely enclosed process challenged device, or PCD, and then the model prediction for the vaporized hydrogen peroxide concentration within that PCD.

And just for reference, the PCD in this case is a sealed polymer tube that contains biological indicators that appear as-- it's like a dark-gray object that you can see within the tubing in the center of the screen there. So basically, after the device component is exposed to the concentration input profile that we're showing on the left, the model can then predict the concentration at interior surfaces, which is shown on the graph on the right.

To do this calculation, however, in addition to the chamber concentration profile, we also need additional information, like geometric information, about the target device or devices as well as material-specific parameters, such as the solubility and diffusivity of vaporized hydrogen peroxide in the various device materials. And typically, we would know the geometry of the device or devices that we're targeting, but what aren't very well established are the relevant material properties that we need as input into the model.

Jon Weeks: Thanks, Dave. Since you said that the relevant material properties may not be well established, Bonnie, can you tell me how we can help to understand these material properties?

Bonnie Liu: Sure. So the material properties that Dave referred to early on are how fast the VH2O2 can diffuse through the material. So since VH2O2 is a vapor, the most straightforward way to experimentally determine this is to measure the vapor penetration through a polymer membrane of each material used in a given device.

An example is shown here on the left-hand side. So here, we have an environmental chamber, which is filled with VH2O2 by evaporation of an aqueous H2O2 solution. After the environmental chamber reaches a stable VH2O2 concentration, a door is opened between the environmental chamber and the device chamber, exposing the device material, which is shown as a green polymer membrane here, 2VHO2.

If the VH2O2 is permeable through the material, it will then reach the device chamber. The concentration of the VH2O2 in both the environmental chamber and the device chamber are recorded independently by VH2O2 probes over time. We can then calculate the diffusion coefficient of VH2O2 through the polymer membrane from the measurement data.

We can then calculate other properties, such as permeation coefficients. However, such an experiment requires specialized equipment, such as the chamber and the VH2O2 probes. It is also time-consuming to set up a measure. For example, it may take a couple of hours to form a stable VH2O2 concentration in the environmental chamber before the polymer membrane could be exposed to VH2O2, and this process needs repeated for each piece of polymer membrane that is analyzed.

Alternatively, in ideal cases, the diffusion behavior is independent of the phase of the sterilant and is only dependent on the movement of the H2O2 molecules. So the same vapor phase properties can be inferred from simple gravimetric swelling studies done in an aqueous H2O2 solution, like what we show on the right-hand side on the slide.

Here, a coupon of the material is immersed in an aqueous H2O2 solution, and we measure its weight gain over time using an analytical balance. Such weight gain can then be plotted against the time, and

the diffusion coefficients can be extracted. We have performed measurements on several device-relevant polymer materials using both methods.

Experimentally, we obtained matching diffusion coefficient results between both methods. We then also validated the theoretical link between the liquid and vapor phase behavior. So this demonstrates that although a vapor phase setup like the one on the left-hand side is more directly relevant to vapor penetration, the simpler, faster benchtop experiment on the right-hand side can actually be used to establish the material diffusion properties needed for the model in much faster way.

Jon Weeks: Dave, can you talk about how we've started validating the computational model that corresponds to the test setup that Bonnie just discussed?

David Saylor: Yeah, sure. So once we have the relevant material properties that Bonnie discussed, we can try to validate the model, and the slide that we're showing currently shows our preliminary results to date. On the left-hand side, we're showing the impact of a complex composite material structure that are structures that are used in many medical devices on the measured permeability of vaporized hydrogen peroxide.

And an example of this are pacemaker leads, which are often comprised of layers of multiple polymer materials, and what this is showing is that using the model, we're able to predict this composite behavior to well within the experimental uncertainty. Then on the right-hand side, we're showing where we've also used the model to predict the behavior of a process challenge device, or PCD, within a sterilization chamber.

And to do this, we compared the model-predicted sterilant dose inside the PCD to the experimentally measured log-surviving fraction and compared this to an experimentally derived dose response relationship. And so what we see is while the experimental uncertainty is somewhat large, our model predictions are quantitatively consistent with those measurements. And I should also mention that this is preliminary. We're currently conducting additional studies to more rigorously assess the validity of this model.

Jon Weeks: Thanks, Dave. Bonnie, what are these additional studies in progress or envisioned to further refine the computational model?

Did we lose you, Bonnie? You might be muted. I think we're having a little bit of technical difficulties.

CDR Kim Piermatteo: Yeah. John, we can't hear her either.

[LAUGHTER]

Jon Weeks: So basically, what we're including for more materials in our experimental measurements, we're looking at additional materials. And like Dave mentioned earlier, we are expanding our experimental efforts beyond single materials. As in a lot of medical devices, there are multiple polymers that are used, and the diffusion is needed to be understood and characterized as its ability to go through those.

We're also embracing a more microbial and activation data from our actual devices or process challenge devices with various composition to further validate our model. I want to thank you both for walking us through the technical details. Since this topic is more research-focused, I'd like to ask you now about the potential applications of the model we've been developing and how this can be used to facilitate adoption of vaporized hydrogen peroxide.

David Saylor: Sure. I'll take this, John. So I think in general, the model could potentially be used to facilitate the development and qualification of vaporized hydrogen peroxide sterilization cycles. I think there are three areas which are shown on the screen here. First, it could potentially be used to get you in the ballpark to directly assess whether a specific cycle parameters will yield adequate inactivation.

And then secondly, for material screening, the model could potentially be used to establish protocols and acceptance criteria for the simple swelling tests that Bonnie described earlier and evaluate whether a particular material is suitable for vaporized hydrogen peroxide sterilization. And the final point there is to potentially leverage the model to assess process challenge devices, or PCDs, to evaluate if the materials and geometry of the PCD are actually conservative with respect to the target devices. So I think those are really the three areas where a model like this could be helpful.

Jon Weeks: Thank you, Bonnie and Dave. And from what I've heard you say, the tools we're developing may be helpful to inform material screening, cycle development, and potentially including process challenge device validation. I'll now turn it over to Ryan to start our final topic for today.

Ryan Ortega: Yeah, thanks for the handoff, Jon. For our final topic, we'd like to share some final updates on our current activities, and then we'll discuss the impact of the town hall series itself and some next steps. And again, although the series is ending, our work on this important topic will certainly continue.

Joining me for this conversation is Scott, Chris, and Tamara to discuss some recent updates. Scott, I'll start with you. Can you tell us a little bit about some of the Tiger Team's analysis to identify materials or maybe devices that might be shifted away from ethylene oxide use to either alternative methods or towards more efficient ethylene oxide use?

CDR Scott Steffen: Yeah, sure, Ryan. As part of our efforts, the Tiger Team took a multifaceted approach to move away from EtO, or ethylene oxide. One approach when the Tiger Team was first established was to perform some internal research, looking in our databases to discover any trends. The high-level analysis of materials and certain devices revealed that there were no simple solutions.

However, the analysis did yield some considerations for industry. I do want to emphasize these are considerations and should not be viewed as guidance. I'll start us off and ask Chris to fill in any gaps as needed. First, regarding validation methods, the half-cycle approach is very commonly used but is very conservative and generally loses more gas than needed.

If firms consider targeting a sterility assurance level, or SAL, of 10 to the minus 6, they may use less EtO. To help achieve this, they may consider using the BI/bioburden or calculated cycle approach. Chris, can you share how the alternative approaches could help?

Chris Dugard: Absolutely. Thanks, Scott. So the BI/bioburden approach can be used to compare the resistance of the actual bioburden of the device with the associated resistance of biological indicators

also used in the load to more accurately tailor the critical parameters to your device. Using the overkill approach guarantees hitting at least an SAL of 10 to the minus 6 while using the BI/bioburden approach gets you closer to an actual SAL of 10 to the minus 6. The cycle calculation approach is very similar, only the BI/bioburden is not used. Only the resistance of the BI is considered.

CDR Scott Steffen: Yeah, thanks, Chris. Second, the idea of alternative sterilization modalities has been mentioned numerous times in our town halls. Several of these alternative sterilization modalities may be appropriate for some devices and materials. With this in mind, we revised our 510(k) sterility guidance, making vaporized hydrogen peroxide an established category A sterilant.

Therefore, firms may want to explore early design considerations with sterilization in mind or explore the changes, if any, that would be needed to move their legacy devices away from EtO. Chris, regarding the 510(k) sterility guidance, can you speak to our recent revision of it and how it impacts the review of devices sterilized using vaporized hydrogen peroxide?

Chris Dugard: Yes, I definitely can. So we recently moved vaporized hydrogen peroxide from an established B modality, in other words, a modality we are familiar with but lacks a recognized standard to establish category A. Thanks to the recent recognition of ISO 22441. This means you can provide the same summary-level information you would for any other established A modality, like steam, ethylene oxide, or radiation. We encourage you to check out town halls three and four regarding these changes for more details.

CDR Scott Steffen: Yeah. Thanks, Chris. One last thought that I would like to bring up for our third consideration is Class I devices. For the most part, CDRH does not see these devices during premarket review. However, many are high volume and could potentially have a meaningful impact on reduced EtO use overall. Firms may want to think about what design considerations for these devices, if any, that could allow for other alternative sterilization modalities to be used. Back to you, Ryan.

Ryan Ortega: Yeah, thanks, Scott. Well, you brought up Class I devices, and so I do want to ask, do either you or maybe Chris have any other device related considerations that people might want to think about.

Chris Dugard: Thanks, Ryan. I can jump in here. So I would like to mention that not all devices need to be sterile, and assessing whether there are any devices in your portfolio that are unnecessarily sterilized could help reduce the use of ethylene oxide and improve efficiency. Aseptic processing of some devices could be considered. We often see devices needlessly sterilized when placed in a kit that has other sterile components. Consider whether some other kitting scheme could be used to prevent that. In all cases, we recommend you reach out to us via Pre-Submission to discuss your specific situation.

In addition to that, our guidance outlines that some devices, like intact skin contacting devices, do not necessarily need an SAL of 10 to the minus 6. We allow an SAL of 10 to the minus 3 for those particular devices. This could potentially reduce the amount of sterilant you need to use on the device. We recommend discussing your specific situation with the Agency if you feel this may be an option for you, and I'll pass it back to you, Ryan.

Ryan Ortega: Yeah, thank you both for sharing some of these technical considerations, but this isn't the only area we've been working in recently. Another one of the many avenues we've been exploring is international harmonization and reliance. We've been engaging lots of interested parties and our

international regulatory partners with goals to explore opportunities that we've mentioned in previous town halls, for example, a reliance pilot. Tamara, can you say a little bit more about this?

CDR Tamara Rosbury: Absolutely, Ryan. CDRH is developing mechanisms for sharing best practices with trusted regulatory partners to facilitate consistent and efficient review practices. The review of sterilization information and changes to sterilization processes are potential avenues we are exploring.

CDRH would be interested in hearing any of our industry-- any industry experiences involving jurisdictional differences in the review and acceptance of sterility information that might be appropriate for discussion with regulatory partners. I would also like to add that international efforts are inclusive of our standards work, recognizing key standards. Back to you, Ryan.

Ryan Ortega: Thanks, Tamara. I'll actually hand it off to Lisa to continue the conversation.

Lisa Simone: Thanks, Ryan. In this panel, I'm joined by Ryan, Tamara, and Scott. All three of you are part of the EtO Tiger Team, and you've all been very involved in the town hall series from the start. So I'd like to hear your perspective on how the town hall series adapted to help us engage with industry and how it helped inform our own internal activities. And I'll start by saying personally, I felt the series was-- it was a great venue for us to discuss new and different concepts and in a new and fresh and exciting way.

So to get us started, I'd like to move to the next slide, which is our familiar arrow timeline. In town hall two, we talked about the creation of the EtO Tiger Team, which is captured a bit left of center in our timeline. Ryan, I'd like to turn to you. You've been involved in activities since then. Would you give us a quick summary of the activities after the Sterigenics closure in 2019 at the lower left that led to the team's creation in March of 2023?

Ryan Ortega: Yeah, sure, Lisa. As a quick refresher for everybody listening, we very quickly implemented several actions that year. We started with the innovation challenges, and then we had our advisory committee meeting in November of 2019. These activities were very quickly followed by our first Master File Pilot Program. Over the intervening years, we were able to implement additional master file pilot programs, and we continued to conduct outreach on these and our other sterilization-related activities. With so much going on, we realized that we needed a central cross-functional group to lead and to coordinate and also to help sustain a focused effort to ship a meaningful subset of medical devices away from ethylene oxide and towards alternative sterilization modalities. So we created the Tiger Team, and the team has not only coordinated the larger center response but also initiated some additional activities as well.

Lisa Simone: Thanks for that quick summary, Ryan. The next questions I'd like to pose to Tamara-- why did CDRH decide to launch the town hall series in January, and what happened during the first two events?

CDR Tamara Rosbury: Great questions, Lisa. The first town hall was intended to be a single event on the fourth anniversary of the 2019 Advisory Committee Meeting. The content quickly expanded into two events, and we talked about the current sterilization landscape, potential supply chain challenges, our activities since 2019, and new activities we were engaging in and preparation for potential changes in use of EtO. All that information is still relevant and captured in town halls one and two.

Lisa Simone: Thank you, Tamara. I'd like to ask each of you about the content and how it might be helpful to interested parties. But first, let's move to a more relevant graphic. This is a screenshot of all of the town hall materials that are available on CDRH Learn. Our moderator, Kim, always shares directions for how to access these town hall materials, so we thought screenshots would provide helpful context for this discussion.

You can see here the town hall number, the topic area, the date, and the associated materials for each event. So after town halls one and two that Tamara described, we began receiving questions about regulatory needs with changes in sterilization, and we knew that the next few events should focus on premarket topics.

So I'd like to turn to Scott. Would you tell us about the scope of these next town halls?

CDR Scott Steffen: Yeah, I'd be happy to, Lisa. When thinking about this question, it makes me reflect on how quickly the agendas for the next three town halls came together. Town hall three gave us a venue to highlight a recent update to our 510(k) sterility guidance. Town hall four, we recognized that to move away from EtO, firms would need to make changes to existing devices. So our review folks shared how to navigate key modification guidances effectively for firms to move forward.

Town hall five gave us a new platform for the recognition of the vaporized hydrogen peroxide standard and two technical information reports. Town halls three through five were designed to provide baseline information to help firms explore their own sterilization needs, including potentially changing sterilization modalities. Back to you, Lisa.

Lisa Simone: Thanks, Scott. We'd only planned five town halls to this point, but based on the feedback, we decided that there was enough interest to extend the series. But we wanted to make sure that the series would continue to provide value. So I'll turn to Tamara and ask, please tell us about the feedback we received and the polling we did to design the content for the rest of the series.

CDR Tamara Rosbury: Sure, Lisa. We received a lot of engagement and questions in nearly every town hall since on different aspects of sterilization changes and potential town hall topics. We started to see themes in the feedback. We offered to polls during our April 29 town hall six event for both potential town hall topics and expanded delivery formats.

As a result of the polling and from feedback from our live Q&A and our mailbox, we developed town hall content in areas that drew strong interest from respondents, including sterility consensus standards, use of master files, including the Master File Pilot Programs, and additional policy incentive structures or regulatory flexibilities.

We also wanted to pivot away from our previous didactic PowerPoint-driven approach, so we changed to a more interactive, conversational, and exploratory format in an effort to better engage the audience. Our goal was to keep people interested and asking questions, and based on feedback we received, we are confident we achieved that outcome. Back to you, Lisa.

Lisa Simone: Thanks, Tamara. I'm interested in Scott and Ryan's thoughts as well. Reflecting back over the series content, how well do you think we did in meeting those content requests?

CDR Scott Steffen: Yeah, absolutely, Lisa. I think we did a great job being nimble and flexible as content suggestions were received. After receiving positive feedback on new consensus standards in town hall five, we were able to discuss with the-- we were able to discuss early recognition of three other consensus standards just a few weeks ago in town hall 14.

As we heard earlier today in topic two, the collaborative research on vaporized hydrogen peroxide penetration was a result of this polling interest. Ryan, what are some of your key takeaways?

Ryan Ortega: Yeah, thanks, Scott. So key takeaways-- we originally gave an overview of our master file pilots in town hall two, and we talked about them more in depth in town hall four. Recently, in town hall 11, we also discussed some practical considerations for people who might be considering the master file pilots.

We also talked about the differences between the master file pilots and traditional device master files. And it was also nice we even shared some reviewer perspectives on best practices for the sterility master files and some of our experiences with those submissions. Also, earlier in the year, town hall three, we talked about our recognition of the new vaporized hydrogen peroxide sterilization and validation standard that you've heard us mention a couple of times today.

We also talked about how it allowed us to revise our 510(k) sterility guidance. And now finally, we're very excited about the flexibilities in the new ethylene oxide sterilization site change guidance that we talked about just earlier today in the town hall.

Lisa Simone: Thanks, Scott and Ryan. Those are some great thoughts. Looking holistically at all of the requests we've received, I also thought we might mention some areas where we weren't able to include specific content in the series. A good example is specific alternative sterilization modalities. So I'd like to turn to Scott and ask why this one was not a town hall topic.

CDR Scott Steffen: Yeah, I would be glad to, Lisa. As you mentioned, we received several requests to discuss specific alternative sterilization modalities. However, as we noted in the past, we are not the experts of those technologies, but we did discuss making device modifications in town halls three and four, considerations for choosing alternative sterilization modalities and town hall seven, material compatibility testing considerations in town halls nine and 10, and biocompatibility assessment considerations related to sterilization changes in town hall 14.

However, we are always interested in learning more about these technologies through options like informational Q-Subs or experiential learning program submissions to help educate CDRH staff. Tamara, you read every email we received in our mailbox. How did we manage other suggestions that weren't ideal for our town hall topics?

CDR Tamara Rosbury: Thanks for asking, Scott. Many questions we received were specific to either a device or a situation and thus appropriate for the respective review division. In some cases, we could respond at the start of a town hall event in the What We Heard segment with a more generalized response that might be applicable to a broader audience.

In addition, we often directed the sender to their review division or to DICE, our Division of Industry and Consumer Education, for specific resources. If you're interested in the questions we've responded to

during previous events, the transcripts are available in CDRH Learn, as our moderator, Kim, will describe at the end of today's event.

Lisa Simone: Tamara, I've got a follow-up question for you. Since today is the last town hall, what advice can we give if folks have questions after today's event?

CDR Tamara Rosbury: Thanks for that question, Lisa. One good resource is town hall 13, where panelists discussed a range of helpful information for medical device innovators, including the broad range of support from DICE. We also talked about the different types of Pre-Submissions and when you might choose one over another. We also talked about SBIR grants.

While we advise you to check out those existing resources through CDRH Learn, our mailbox will remain open for questions or comments as you continue to explore reducing reliance on EtO and potentially switching to alternative sterilization modalities.

Lisa Simone: Thanks for that, Tamara. When our town hall six polling suggested a pivot to more interactive panels like this one, we received strong feedback for a particular format that turned out to be one of our favorites. And for that video format, I'd like to pass it to Ryan.

Ryan Ortega: Yeah, thanks, Lisa. With a prompt like that, you can only be talking about our mock Pre-Submission that we did back in town hall nine. Like you mentioned, we had received feedback that folks were interested in something more interactive for our formatting. So we basically took something that we had tried on a smaller scale, and we adapted it to our town hall series.

Essentially, what we did was to show an example of what a Pre-Submission looks like using FDA personnel to play both the company and the FDA review team. The mock Pre-Sub covered questions about changing sterilization modalities so we could use that as an example of a Pre-Sub meeting and also share some best practices and also to share some technical thoughts about sterilization changes too.

From my own personal perspective, it was pretty fun to change up the format a little. I hope it was engaging for the audience too. We received a lot of positive feedback about it, which to me indicates that it was responsive to the requests that we had received to have more engaging or interactive content in the town halls and the interest that people had expressed in hearing about changing sterilization modalities and potentially exploring some case studies.

Lisa Simone: Thanks, Ryan, for sharing one of our favorites. The town hall nine mock was a great example of a type of case study that we can do without revealing proprietary information. Town hall 14 also included a case study for the recognition of the consensus standard, ISO 11737-3, for bacterial endotoxin testing. In that town hall, our panelists described the steps that CDRH took after we received two recognition requests from interested parties through the publication in our Consensus Standards database.

At this point, we haven't mentioned every topic in every town hall shown here, but I'd like to visualize the series in a different way as we share some final thoughts.

Next slide, please. These are the topics discussed over the 15-event series grouped by subject area. And we won't step through each of these, but I'd like to ask our panelists to share their thoughts on the content and perhaps on the value that might not be so obvious.

And I'll kick it off by sharing that as a lead for the sterilization response effort, the series allowed us to get broad feedback on the challenges and the progress that you, our audience and industry partners, have experienced, and that's helped inform the Tiger Team activities that we pursued and that we're still pursuing. For more thoughts, let me turn it over to Tamara.

CDR Tamara Rosbury: I'd like to echo Lisa's remarks on your feedback. We sincerely express our gratitude for your participation in the town hall series and have worked hard to be responsive to your needs. Participant feedback allowed us to quickly respond to topics you were eager to hear about from FDA.

For example, after receiving several inquiries about predetermined change control plans, or PCCPs, we initially responded via the What We Heard segment, and later, in town hall 12, we convened a panel of FDA experts to develop a short discussion topic on PCCPs. We also had requests to discuss bundling of sterility submissions, which we included in town hall 13. Ryan, do you have anything to add?

Ryan Ortega: Yeah, I do. Drawing again from my own personal perspective, I think the discussions that we had on some of our flexibilities, like the master file pilots, helped to stimulate interest, and very importantly-- I think you're hearing a theme here-- folks have been reaching out to us to share their perspectives and feedback. I feel-- and I hope our audience does too-- that we've striven to be as open and as transparent as we can be about our different initiatives in this area.

And the town hall series has been just a really excellent tool for providing news and updates throughout the year. I'll also say that the town hall series has been a great venue for talking about new and updated guidances or maybe providing a refresher on existing guidances. It's just really valuable to be able to discuss our guidances in this venue where the specific recommendations in the guidance can be presented within the context of our specific work on sterilization innovation.

And we can also highlight the interconnectivity of all of this good work. Just as an example, our lessons learned from the innovation challenges in the advisory committee meeting helped us to make the first master file pilot, and that, in turn, led to the subsequent pilots. Then the things that we learned in those pilots helped inform our thinking on the new ethylene oxide sterility site change guidance.

None of these things would have happened in a vacuum, and the town hall series lets us show that while also continuously inviting that feedback that's so crucial to our ongoing work. Scott, do you have any reflections or maybe overarching thoughts that you'd like to share?

CDR Scott Steffen: Yeah, Ryan, that was some great feedback you just gave. So from my perspective, I think this slide is a great way to view the broad town hall content by a topic area. And if you were trying to explore any particular topic, and then you can leverage the CDRH Learn information on the previous slide to see which town hall covered the content that you were interested in.

We tried really hard to incorporate topics that provide value to you, the audience, and also to our review staff. A great example is in the upper left with premarket and standard topics. We were able to

share a range of new standard recognitions which reduce the burden of review. Lisa, we've mentioned collaboration several times during our town hall series. Are there any specific examples you'd like to highlight?

Lisa Simone: Thanks, Scott. We could go on about all the different collaborative ideas and challenges, but I'll just focus on two. The current sterilization landscape really represents a range of challenges and opportunities that are best addressed by working together. And a great example is the vaporized hydrogen peroxide collaborative research that Jon and Dave and Bonnie shared in topic two, and that was developed through an industry partnership called a research collaborative agreement, or an RCA.

The second example I'll give is our announcement of CDRH's participation in the Kilmer Community on Sterility Assurance. These collaborative communities are continuing forums where public and private-sector members proactively work together to achieve common objectives and outcomes, for example, peer-reviewed content and precompetitive data sharing that supports large and small manufacturers. CDRH is looking forward to participating in the Kilmer Community on Sterility Assurance.

So as we bring this discussion to a close, I'd like to thank our panelists and also our listening audience who've traveled so far with us over the last year. We recognized early on that we didn't have all the answers and that collaboration and communication, both internal to the Agency and external, is key. And we want to build on the momentum that the town hall series generated, and we'll talk more about what that might look like in our final panel discussion on next steps. And for that, let me turn it over to Tamara.

CDR Tamara Rosbury: Thanks, Lisa. Our panelists will now address the question, looking forward, what activities might we continue to engage in as an industry to reduce reliance on EtO and increase resiliency in the sterilization landscape? The town hall series is ending because the goal to level-set information and engage participants has been successful.

Participants are talking. Collaborations are ongoing, and new efforts have launched. Participants are actively engaged, and many areas exist for continued efforts. I'd like to ask our panelists today about their thoughts as we look to the future within the scope of their current activities. Jon, can you get us started on OSEL's activities?

Jon Weeks: Yes, thank you, Tamara. In OSEL, we're continuing research activities in this area. CDRH and OSEL are interested in developing research collaboration agreements, like the one we've discussed today, to help address regulatory science questions. We are exploring what additional regulatory science considerations might inform the adoption of different sterilization modalities.

In addition to research activities, CDRH also remains interested in standards. This includes continued activities and input for standards development and recognition activities for alternative sterilization modalities. CDRH has been very involved in efforts to advance the development of consensus standards related to sterilization.

In Town Hall 14 a couple of weeks ago, we talked about the task force CDRH created to help inform and integrate our FDA liaisons and subject-matter experts involvement in standards development to support timely recognition and new initiatives. We encourage interested parties to get involved in SDO

development and recognition, as recognized standards that are globally harmonized can help the medical device industry and patient access to life-saving technologies. What are your thoughts, Lisa?

Lisa Simone: Thanks, Jon. I'm going to keep beating that drum for encouraging collaboration and communication. You mentioned RCAs, and I'd like to share that our Division of Partnerships and Innovation, or DPI, helps us develop and sustain collaborative partnerships that support innovation and regulatory science advancements, for example, through the participation in collaborative communities like that Kilmer Community I mentioned earlier.

We also encourage those of you with expertise to collaborate in the education of our CDRH staff on important sterilization topics. In town hall 13, we talked about our Experiential Learning Program and our informational Q-Sub Program. Also, we welcome the opportunity to continue participating and collaborating with you in relevant conferences and workshops. And now I'd like to pass it to Aftin for her final thoughts.

Aftin Ross: Thank you, Lisa. A common theme we heard during the town halls and as we have been engaging across the ecosystem is around opportunities for international collaboration. In addition to the standards efforts that Jon mentioned, CDRH is developing mechanisms for sharing best practices with trusted regulatory partners to facilitate consistent and efficient review practices.

For example, review of sterilization information and of changes to sterilization processes is one potential avenue we are exploring. Recognizing we don't have all the answers, CDRH be interested to hear of any industry experiences involving jurisdictional differences in review and acceptance of sterility information that might be appropriate for discussion with regulatory partners.

During the town hall series, we've also discussed a wide range of FDA sterilization resources. As the sterilization ecosystem continues to evolve, please continue to make use of resources such as the EtO Master File Pilot Programs and our recently released EtO site change IIE guidance, which was highlighted at the outset of our town hall today.

I will now pass it to my colleague, Tammy Beckham, to share more about the work FDA has been doing to ensure patients and providers continue to have access to the sterile medical devices they need.

Tammy Beckham: Thank you very much, Aftin. As you mentioned, we've been working very diligently to ensure that patients and providers have access to sterile medical devices that they need at the time that they need them. FDA is continuing to conduct, as we have been, extensive outreach to sterilizers, manufacturers, and other medical device-interested parties.

We're monitoring progress toward implementation of EPA's National Emission Standards for Hazardous Air Pollutants, or NESHAP, progress toward implementing those requirements, and we're also having discussions about potential challenges as well for implementing those requirements. And as everyone knows on this call, when facilities do close, even if it's on a temporary basis, for facility upgrades, there can be downstream impacts for patients resulting from unavailability of sterile devices.

So to that end, we continue monitoring the supply chain and sterilization landscape, and as I said, we continue to engage with manufacturers and sterilizers so that we can help prevent and mitigate medical device shortages. If manufacturers are experiencing any disruptions in sterilization that are likely to lead

to a meaningful disruption in availability of a device, please contact the CDRH Office of Supply Chain Resilience, and submit a notification through the 506J process.

The link to submit notifications is included in the resources at the end of the presentation. Providers, healthcare systems, patients, and others can also submit information about supply chain disruptions and shortages to the Device Shortages mailbox, which will be also shown on the next slide. Back to you, Tamara.

CDR Tamara Rosbury: Thank you, panelists, for a very robust discussion on industry engagement to reduce reliance on EtO and increase resiliency in the sterilization landscape. We at CDRH continue to work on current sterilization-related challenges, even as the town hall series is ending.

Again, our mailbox is still active going forward if you have any follow-up questions related to the town hall series or the current sterilization related topics we've discussed. For any real or potential supply chain challenges, please reach out to our Office of Supply Chain Resilience, or OSCR. Listed here is contact information for OSCR and DICE. Any new information will appear on our Sterilization website listed here. Lisa, I'll turn it back over to you.

Lisa Simone: Thanks, Tamara. The next three slides include resources mentioned earlier in the presentation along with the full URLs that you can access after the presentation.

Now, we know today has been a long day and we've covered a wide range of topics, but as just a quick summary, we discussed the new "Transitional Enforcement Policy for Ethylene Oxide Sterilization Facility Changes for Class III Devices" guidance. We believe that the enforcement discretion policy set forth in the newly released guidance may help address urgent public health concerns related to potential sterile medical device shortages impacting certain devices sterilized by EtO. We also shared research and modeling on diffusion of vaporized hydrogen peroxide through select polymeric materials, and we also discussed the scope and impact of the sterilization town hall series and explored next steps. And now I'll turn it back over to Kim.

CDR Kim Piermatteo: Thank you, Lisa, and thank you to all of our panelists for the great discussions today. We'll now transition to our question-and-answer segment. I do want to let everyone know that we have a shortened time for question-and-answers, so I encourage you to start thinking about your questions, raise your hand, and get into the queue as soon as possible to engage with our panelists.

Just so you know, as like in previous town halls, I'm going to go over how we'll manage this segment. So to ask a question or to 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. Please identify yourself and your organization, and then ask your question or provide your comment. After you ask your question or provide your comment, please lower your hand. And then if you have another question or comment, please raise your hand again in Zoom to get back into the queue, and I will call on you as time permits.

So as you gear up your questions, I am going to ask one question to Bella before we take our first live question, and Bella, that question is, why was the EtO site change IIE guidance published as an immediately-in-effect guidance?

Bella Pelina: Thanks for that question, Kim. I want to start off by mentioning that although this guidance is being implemented without prior public comment, it still remains subject to comment in accordance with the Agency's good guidance practices. With that being said, why was this guidance published as an IIE guidance? Well, FDA determined that prior public participation for this guidance is not feasible or appropriate because immediate implementation is needed to help protect the sterile device supply chain.

To add to that, FDA believes that the enforcement discretion policy described in this guidance will provide an option for facilities that can help them prevent and mitigate possible interruptions in sterile device processing and help maintain adequate supplies of finished sterile medical devices during the time period that manufacturers are transitioning to compliance with new EPA requirements.

CDR Kim Piermatteo: Thanks, Bella. Again, please, I encourage you to raise your hands to engage with our panelists today. There are quite a few experts here, so I encourage you to think of questions, comments and engage with our panelists today. Next, though, I think then I'll go to Lisa with another question, and Lisa, that question is, with the town hall series ending, does this mean a ramp-down on FDA activities associated with the current sterilization challenges? Would you consider additional town halls? And how do you plan to convey new updates going forward?

Lisa Simone: That's a great question, Kim. Thanks. The town hall series was really just one way that we've sought to engage stakeholders with discussions on reducing reliance on EtO and thinking about those alternative modalities. And we think the series has covered a broad range of topics, and it's launched other activities and conversations, some of which we talked about today.

And as we look to the future, we'll explore more of those forward-looking activities, but at the moment, we aren't planning another town hall. But we recognize there may be value in future discussions. So to answer your first question, no, this does not stop any of our work. It continues, and we'll leave the door open for future possibilities if needed for another town hall. Thank you.

CDR Kim Piermatteo: Thank you, Lisa. Okay, I don't see any raised hands, but again, I encourage our attendees to engage with our panelists. I think then I'm going to jump to ask Jhumur question, and Jhumur, that question is, how long will the enforcement policy identified in this EtO site change IIE guidance be available?

Jhumur Banik: Thanks, Kim. So based on our understanding of the potential impact on sterilization activities, as facilities come into compliance with EPA's rule and potential future action on interim decision for EtO get finalized, FDA anticipates this enforcement discretion policy will likely no longer be appropriate after three years, and therefore we anticipate declining any requests after that time. But if this view changes, FDA intends to revise this guidance, whether it means to extend, modify, or replace the policy in this guidance.

CDR Kim Piermatteo: Thanks, Jhumur. Okay, I think I'm going to-- again, please, I do encourage you-- we have about 10 minutes left. I encourage you to engage with our panelists or we're going to keep going through some questions that we've previously received. The next question, I'm going to direct that one-- I'm going to direct that one to Bonnie, and Bonnie, that question is, how can this model be used as part of sterilization validation?

Bonnie Liu: Sure, that's a great question, Kim. So first, please note that this is the first iteration of the model, and we intend to refine it as more actual use data becomes available to us. So with that context in mind, the model can be used to determine whether the sterilant will penetrate through the material of construction and for the initial design of a sterilization cycle.

The model can predict whether the achieved concentrations are within the ballpark of the sterilization conditions. We would recommend that manufacturers conduct validation testing in accordance with the appropriate consensus standard ISO 22441.

CDR Kim Piermatteo: Thanks, Bonnie. Alright, I still do not see any raised hands, so I am going to come to Tammy next. Tammy, I'm going to ask you a question related to this town hall series wrap-up, and that question is, does FDA have a better understanding of the potential shortages in medical devices as a result of industry outreach? Can you share how the Agency can support the industry responding to these challenges to bolster the resilience of the sterilized medical device supply chain?

Tammy Beckham: Sure. As you know and as I said previously, FDA continues to proactively engage with industry since 2019, and we are aware of potential challenges that could impact availability of medical devices. Based on information that's been shared, we have conducted an impact assessment to understand potential patient impact and supply chain impact. Our assessments are then used to utilize and inform implementation of both regulatory and nonregulatory mitigations. So once we know that there could be a potential issue, obviously we do that impact assessment, and then we use that impact assessment, like I said, to inform both regulatory and nonregulatory mitigations.

Regulatory mitigations includes letters to healthcare providers, expedited 510(k)'s, 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 about different types of mitigations that are nonregulatory in nature. So as an example, though FDA doesn't have delegated authorities under the DPA, 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.

CDR Kim Piermatteo: Thanks, Tammy. Alright, I think then I see no more raised hands. If you have a question or a comment, please quickly raise your hand. I'm going to ask one more question to our panelists, and if there are no raised hands, then we will move to wrap up. This question I'm going to direct towards Jon regarding VHP. And so, Jon, the question is, how does CDRH engage with external groups to address research gaps needed to answer regulatory questions?

Jon Weeks: Thanks, Kim. CDRH engages with external groups through various mechanisms, including materials transfer agreements, research collaboration agreements, and collaborative research and development agreements. In the Office of Science and Engineering Laboratories, we are engaged in several research collaboration agreements with industry partners, such as what we described today. We are commonly looking for future opportunities for development of research projects and other collaborations. Additionally, there are also funding opportunities, such as the National Science Foundation Scholar-In-Residence and Small Business Innovation Research. Please refer to town hall 13 for more information about SBIR opportunities.

CDR Kim Piermatteo: Thanks so much, Jon. Alright, I do not see any more raised hands, so that will wrap up our comment and question-and-answer segment. Thank you all for attending and thank you especially to our panelists for all of their work in presenting this material to you today and addressing these questions. I'd now like to turn it back over to Lisa to provide her final thoughts for today. Lisa?

Lisa Simone: Thanks, Kim, and Thanks to everyone for joining us today for our last Sterilization Town Hall. We very much appreciate your active engagement over the last year, and thanks for coming together today to talk about the incentive structures over the years, the value of standards and recognition, of education, of information sharing, and I keep beating that collaboration drum. We're looking forward to the new innovations and collaborations, including those you've already begun, so keep in touch. Thanks again for joining us, and now I'll turn it back over to Kim.

CDR Kim Piermatteo: Thanks, Lisa. And before I close out, I would just like to again thank the CDRH EtO Tiger Team for all their hard work over the last year in preparing for these town halls and presenting exceptional information regarding medical device sterilization and for all of you for attending and participating in these town halls.

For me, as usual, I just want to mention printable slides of today's presentation are currently available on the Events page for this town hall and CDRH Learn. A recording of today's town hall and a transcript will be posted to the Events page and CDRH Learn in the next few weeks, and a screenshot of where you can find these materials on CDRH Learn has been provided on this slide.

As mentioned earlier, if you have any additional questions or comments about medical device sterilization or this town hall series, please email medicaldevicesterilization@fda.hhs.gov. And even though the series is coming to an end, we hope you come back and join us for other CDRH webinars or town halls, and you can find a listing of all these upcoming events on our CDRH events page at www.fda.gov/cdrhevents.

Thank you all again for joining us for this town hall series on medical device sterilization. We greatly appreciate your participation and engagement. This concludes our town hall for today.

****

END