

SUMMARY MINUTES

**CENTER FOR DEVICES AND RADIOLOGICAL HEALTH
GENERAL HOSPITAL AND PERSONAL USE DEVICES PANEL**

November 6, 2019

**DoubleTree by Hilton Grand Ballroom
Washington DC North/Gaithersburg
620 Perry Parkway
Gaithersburg, MD 20877**

Attendees:**Temporary Voting Chair**

Frank R. Lewis, Jr., M.D.
Executive Director, Emeritus
American Board of Surgery

Voting Members

Robert E. Burr, M.D., M.Sc.
San Juan Regional Medical Center
Farmington, NM

Lisa Gualtieri, Ph.D., Sc.M.
Tufts University, School of Medicine
Boston, MA

Michael A. Saubolle, Ph.D.
University of Arizona, College of Medicine
Phoenix, AZ

Charity J. Morgan, Ph.D.
University of Alabama
Birmingham, AL

Avery Tung, M.D.
University of Chicago Medicine
Chicago, IL

Eugene S. Kim, M.D.
Children's Hospital
Los Angeles, CA

Temporary Voting Members

James W. Collins, RN, CNOR
Cleveland Clinic
Lorain, Ohio

Sandra Myers, D.N.P.
Baptist Health Corbin
East Bernstadt, KY

Teresa Wells, RN, B.S.N., M.B.A.
Department of Veterans Affairs
Washington, DC

Gary Socola
HIGHPOWER Validation Testing & Lab Services, Inc.
Rochester, NY

Lynn R. Goldman, M.D., M.S., M.P.H.
The George Washington University
Washington, DC

Michael Yaszemski, M.D., Ph.D.
Mayo Clinic
Rochester, MN

Ashley Faulx, M.D.
Case Western Reserve University
Cleveland, OH

Daryle Gardner-Bonneau, Ph.D.
Bonneau and Associates
Portage, MI

Stephen Li, Ph.D.
Li Consulting
Palm Harbor, FL

Stephen Wilcox, Ph.D.
Design Science
Philadelphia, PA

Matthew Arduino, Dr.P.H.
Centers for Disease Control and Prevention
Atlanta, GA

Isaac Benowitz, M.D.
Centers for Disease Control and Prevention
Atlanta, GA

Jason Dominitz, M.D.
Department of Veterans Affairs
Seattle, WA

Industry Representative

Carol Pekar, M.B.A., RAC
Carol Pekar Consulting LLC
Stow, MA

Consumer Representative

Keziah (Kate) Sully, M.D.
Interventional Psychiatrist
Pensacola, FL

Patient Representative

Debra Dunn
Patient Advocate
Libertyville, IL

Designated Federal Officer

Patricio Garcia, M.P.H., CDR, USPHS
Food and Drug Administration
Silver Spring, MD

CDRH/OST

Suzanne Schwartz, M.D.
Office Director (Acting)
Food and Drug Administration
Silver Spring, MD

CDRH/OPEQ/OHT-4

David Krause, Ph.D.
Deputy Office Director
Food and Drug Administration
Silver Spring, MD

CDRH/OPEQ/OHT-3

Ann Ferriter
Associate Director
Food and Drug Administration
Silver Spring, MD

REDUCTION OR ELIMINATION OF ETHYLENE OXIDE EMISSIONS FOR MEDICAL DEVICE STERILIZATION

CALL TO ORDER

Panel Chairperson Frank R. Lewis, Jr., M.D., called the meeting to order at 8:01 a.m. He noted the presence of a quorum and stated that the Panel members had received training in FDA device law and regulations. He announced that the Panel would be discussing the topic of industrial ethylene oxide sterilization of medical devices, its role in maintaining public health, and the reduction or elimination of EtO emissions.

INTRODUCTION OF THE COMMITTEE

Chairperson Lewis asked the Panel members and the FDA staff to introduce themselves.

CONFLICT OF INTEREST STATEMENT

Patricio Garcia, M.P.H., CDR, USPHS, Designated Federal Officer, read the Conflict of Interest statement and reported that no conflict of interest waivers had been issued.

He introduced Carol Pekar as the Industry Representative.

He then made general announcements to the public regarding transcripts and videos and introduced Sandy Walsh as the FDA press contact.

INTRODUCTION AND INTERNATIONAL PERSPECTIVE

FDA/CDRH Opening Remarks

Ryan Ortega, Ph.D., Surgical and Infection Control Devices, welcomed the attendees and thanked the FDA staff, the Panel members, and all stakeholders. He announced that the one and a half day meeting was being held to address issues relating to industrial ethylene oxide sterilization and reduction of the risk of infection from duodenoscopes. He related that FDA has been working with multiple stakeholders in ensuring against medical device shortages due to the closure of the Sterigenics sterilization plant in Willowbrook, Illinois. He acknowledged that many concerns have been raised regarding the potential for shortages of critical sterile medical devices as well as the risks related to EtO exposure in the air around sterilization facilities. He reviewed the steps FDA is taking to address these issues, recognized the public's concern regarding unsafe environmental levels of ethylene oxide, and confirmed FDA's responsibility to safeguard the availability of sterilized medical devices for patients throughout the United States.

EPA/OAQPS Opening Remarks

Michael Koerber, Deputy Director, Office of Air Quality Planning & Standards at

EPA, provided an overview of EPA's statutory authority under the Clean Air Act. He explained what the National Air Toxics Assessment is and how it is used as a screening tool to help identify areas, pollutants, or sources that need further examination for a better understanding of risks to public health. He revealed that the most recent assessment found several areas that have potentially elevated cancer risks from long-term exposure to ethylene oxide and that it is more potent than what was previously known. He then outlined EPA's approach to addressing ethylene oxide emissions, noting that this will include a review of Clean Air Act regulations and the gathering of information on industrial emissions to support regulatory review.

CDC/ATSDR Opening Remarks

Christopher M. Reh, Ph.D., Associate Director, Agency for Toxic Substances and Disease Registry at CDC, provided background information on ATSDR's mission, responsibilities, and activities. He explained that ATSDR's work includes reduction of community exposure to poisonous substances; building a science base on hazardous materials; and educating communities, health care providers, and the public about toxic chemicals. He then covered the agency's recent involvement with ethylene oxide, noting that an evaluation of EtO concentrations in Willowbrook, Illinois, led to the conclusion that there may be an increased cancer risk to some people in the community. He also described additional activities and challenges, noting that there is a need to better identify and quantify all EtO emissions to better understand their impact on communities.

UK Perspective on Industrial EtO Medical Device Sterilization

Andrew Bent, B.Eng. (Hons), C.Sci., MTOPRA, provided background information on the Medicines & Healthcare products Regulatory Agency, including its role, the scope of its activities, and its responsibilities. He also reviewed medical device definitions, classifications, and regulations in the UK. He then discussed standards and directives covering the use of ethylene oxide, noting that BS EN ISO-11135 is the predominant standard for EtO in Europe and the UK. He covered its scope, inclusions and exclusions, and requirements. He also noted that other methods not covered in the international standards are used to determine residual EtO levels, biocompatibility aspects, and good practice guidance through the application of normative requirements.

FDA'S OVERSIGHT OF MEDICAL DEVICES AND THEIR STERILITY

Shortage of Ethylene Oxide Sterilized Medical Devices: CDRH's Role

Adam E. Saltman, M.D., Ph.D., Office of Product Evaluation and Quality, discussed how and why shortages happen. He explained why gaps between supply and demand in the medical device market can become significant and sometimes permanent, and he gave examples of circumstances that could cause the need for products to exceed the quantity at hand. He then looked at CDRH's approach to potential shortages, which include deficit assessment, determination of medical necessity, and development of a management

plan. He also provided examples of regulatory and communication tools that are used to help mitigate shortages, such as economic and logistical analyses, expedited reviews, public notifications, and information exchange.

Shortage of Industrial Ethylene Oxide Sterilized Medical Devices: Clinical Impact

Karoll J. Cortez, M.D., M.H.S., FACP, Surgical and Infection Control Devices, discussed the clinical ramifications of medical device shortages. She noted that over 50% of all sterile medical devices rely solely on ethylene oxide sterilization, because in many instances, other validated methods can lead to degradation of materials. She walked the Panel through a recent example of a tracheostomy tube shortage to illustrate the issues related to these events and explained that the severity of clinical impact depends on device type and intended use, patient population, misallocation and hoarding of devices, and effectiveness of mitigation measures. She emphasized that the unavailability of essential medical devices can prevent physicians from making diagnoses or from performing lifesaving interventions and that prompt action can reduce or prevent these adverse consequences.

Overview of Industrial Ethylene Oxide Sterilization

Steven Elliott, M.Sc., Surgical and Infection Control Devices, described the status of ethylene oxide for the industrial sterilization of medical devices. He cited a number of reasons for its use; these include broad material and device compatibility, process flexibility, and a long history of use and regulatory familiarity. He explained the characteristics of an ethylene oxide sterilization cycle, noting that factors such as dimensions, materials, load density, packaging types and amounts, type and quantity of microbial contamination, and load configuration all contribute to the ease or difficulty of sterilizing a load of medical devices. He then gave an overview and description of the elements that are involved in EtO sterilization process authorization.

How FDA Reviews Sterilization Information in Premarket Regulatory Submissions for Medical Devices

Christopher Dugard, M.S., Surgical and Infection Control Devices, explained the differences between industrial and healthcare sterilization. He provided an overview of how FDA reviews sterilization information and what is needed to support a premarket submission. He then discussed FDA's sterility guidance, its regulation of the process, and additional requirements, such as labeling and product life cycle specifications.

CLARIFYING QUESTIONS FROM THE PANEL

Chairperson Lewis asked to what extent ethylene oxide sterilization could be replaced by gamma radiation. **Mr. Elliott** replied that a lot of testing is required to determine whether certain devices may have compatibility with other processes and that there is a burden associated with changing from one modality to another.

Chairperson Lewis then asked if there are obvious types of devices for which radiation sterilization is not satisfactory as a replacement for ethylene oxide. **Mr. Elliott** replied that there are. He explained that radiation-based sterilization processes are deep penetrating and can have an impact on device materials that could compromise integrity.

Chairperson Lewis asked Dr. Saltman how severe he believes the situation is with regard to industrial sterilization. **Dr. Saltman** replied that the issue has been that the supply was limited and that now, because of the shutdowns, any capacity has been fully utilized, making it more difficult for manufacturers to find other sites.

Robert E. Burr, M.D., MSc., asked what abatement systems are currently being used and why they are not effective. **Mr. Koerber** indicated that the problem is not necessarily noncompliance with EPA standards; emission standards are dated, and assessment of the updated cancer potency value identified a number of communities that are at risk for elevated cancer, which has caused a reaction from people in those communities who did not know about the existence of the facilities.

Chairperson Lewis asked if similar data have been collected from other facilities. **Mr. Koerber** responded that the most recent assessment identified 20 areas with the potential for elevated cancer risk and that EPA is working with state and local air agencies to gather more information to better understand the risk.

Avery Tung, M.D., asked if this is a problem with all sterilization facilities. **Mr. Koerber** replied that the EPA is still learning about the extent of the problem, that its focus is on the higher-risk areas, and that more progress needs to be made.

Gary Socola asked if the methodology for the 2014 NATA assessment was validated and by whom. **Mr. Koerber** replied that non-regulatory assessments do not go through a formal peer review. He reiterated that the purpose is to highlight those areas that may be at potential elevated risk and that the initial results are not necessarily a cause for action but for further investigation.

Jason Dominitz, M.D., asked for comment on the occupational exposure and health effects. **Dr. Reh** responded that NIOSH has a current intelligence bulletin on EtO as well as documents on reducing exposures in the sterilization industry and that it has also done some occupational epidemiology studies.

IMPACT OF CONTRACT STERILIZATION ON MEDICAL DEVICE SUPPLY CHAINS

Manufacturer Perspective of Medical Device Supply Chains and Device Sterilization

Mark B. Leahey, J.D., President and CEO of the Medical Device Manufacturers Association, shared the results of a recent survey of its members on EtO sterilization. He reported that 94% of its members indicated that if their primary sterilization facility were to go offline, they would have shortages. In addition, a majority stated that no current alternatives to EtO sterilization exist for their devices, and critical products such as surgical kits, catheters, and feeding tubes would be impacted. He then gave an overview of how devices go through the supply chain and discussed points of consideration when changing sterilization modalities. He indicated that the next steps would include enhanced collaboration among FDA, industry, and sterilization facilities on alternatives to the current

process; opportunities for FDA to provide streamlined ways of transitioning to alternatives; and consideration of the impacts of any proposed changes.

Group Purchasing Organization Perspective of Medical Device Supply Chains and Shortages Due to Loss of Sterilization Capacity

David Gillian, Senior Vice President of Supply Chain Operations for Vizient, described the impact that the sterilization issue is having on healthcare providers and discussed the steps that are being taken to diminish potential disruptions to the supply chain. He explained how the supply chain model works and cautioned that limited sterilization capacity will form a critical choke point for medical supply products, creating a different type of shortage than what has been experienced before. He related that member hospitals have indicated that limited access to the use of EtO will have dramatic consequences and that a ban will essentially shut down operating rooms across the country. He further commented that many stakeholders are doing what they can to mitigate the potential supply disruption, that there is no easy or quick fix, and that a thoughtful, measured, and transparent approach should be taken to address these issues.

Healthcare Delivery Organization Perspective of Potential Impact on Patients Due to Loss of Medical Device Sterilization Capacity

Kara Mascitti, M.D., St. Luke's University Health Network, stated that various healthcare systems throughout the country have reported disruptions of critical life-sustaining supplies and have had to allocate additional time, labor, and financial resources to finding alternatives. She stated that she is concerned that if sterilization facility closures continue without adequate warning or contingency plans, patient safety will be at risk and unnecessary harm will occur. She pointed out that in-house sterilization by hospitals and health systems would be prohibitive in terms of cost and logistics and that inadequate sterilization would be catastrophic for patient care. She maintained that changes to sterilization methods must occur in a coordinated and systematic manner to minimize unintended consequences. She urged FDA to continue working collaboratively with stakeholders to develop a coordinated, cohesive, and systematic approach to addressing these concerns while carefully considering the unintended negative consequences that sterilization facility closures would have on patient care.

REDUCING ETHYLENE OXIDE EMISSIONS FOR MEDICAL DEVICE STERILIZATION

Overview of EtO Sterilization Process and Engineering to Optimize EtO Use

Phil Cogdill, Medtronic, gave a detailed review of the sterilization process and discussed the following key points:

- Sterilization starts and ends with the patient.
- Sterilization is not just about eradicating microorganisms.
- Ethylene oxide sterilization is a highly controlled process.

- New approaches may allow for reduction in the amount of EtO gas in the industrial process.

He then presented suggestions for better utilization of EtO, such as reduction of paper materials in packaging, elimination of paper IFUs, and consolidation of the number of cycles into optimized rotations. He noted that EtO sterilization processes are complex and lengthy; few products sterilized by ethylene oxide can move to other modalities; and changes to sterilization processes are difficult and take time.

Reduction of EtO Emissions by Changing Cycle Design and Validation Methods

Brian McEvoy, B.Sc., M.B.A., STERIS Applied Sterilization Technologies, discussed topics related to the reduction of EtO use and emissions, including maintenance of an acceptable assurance of sterility, changes in cycle parameters, and challenges in implementing new cycle designs and validation methods. He acknowledged that opportunity exists within the current methods to be more efficient, and he looked at the impact that a lessening of EtO concentration could have on process parameters, noting that a 50% reduction in concentration will yield a greater than 50% decrease in residuals. He stated that sustainable EtO validation techniques will present opportunities to optimize the process in the most efficient manner while continuing to deliver required sterility assurance in accordance with internationally recognized standards.

Reducing EtO Use in Sterilization Cycles by Changing Sterilization Load Configuration

Dennis Christensen, the owner of SVC, a contract EtO facility, provided background information on the history of sterilization and looked at potential ways of reducing the use of ethylene oxide. He stressed the need for placing biological indicators in the most difficult areas for gas to get into, and he highlighted the benefits of BI/bioburden; these include less EtO per cycle, shorter exposure time, and lower residuals. He discussed the importance of the fractional run for validation and looked at the impacts that product packaging, the weight of cardboard boxes, pallet configuration, and stretch wrap can have on the sterilization process. He also suggested that a lower D value biological indicator for ethylene oxide sterilization would result in reduced exposure time for all EtO cycles.

Flexible Chamber EtO Sterilization

A.E. Ted May, President and CEO of Andersen Products, discussed the characteristics of ethylene oxide flexible chamber technology, fundamental differences between rigid and flexible chambers, industrial applications of EO-FCT systems, and how these systems can help reduce EtO emissions. He explained that the use of fixed metal chambers in traditional sterilization processes results in significant dead space that necessitates the use of large amounts of ethylene oxide to achieve high gas concentrations. Conversely, the use of flexible bags that collapse around the load eliminates all dead space, achieving high gas concentration with very small amounts of gas. He then presented three

case studies showing the benefits of in-house and third-party sterilization. He concluded that EO-FCT sterilization is an established method, that the cycles are very gentle, that it is an attractive option for small and medium device manufacturers, and that it is the most gas-efficient system currently available.

Clarifying Questions from the Panel

Chairperson Lewis asked what the best method is to implement all of the suggestions into the industrial process in order to achieve practical utilization. He also asked what the roles of FDA, EPA, or other organizations would be in facilitating it. **Mr. Cogdill** replied that Medtronic submitted three innovation challenges to the FDA and is collaborating with a number of leading companies on getting publications out.

Chairperson Lewis asked him if he believes that the current studies are adequate and if a publication will achieve this without needing a greater degree of oversight and management of the processes. **Mr. Cogdill** replied that anything the company can do to reduce the potential exposure and emissions is a benefit and that it falls within its mission statement. **Mr. McEvoy** confirmed that STERIS is following the ISO standard and has been openly presenting its approach to the sustainability program across industry.

Eugene S. Kim, M.D., asked if like products could be bundled together for sterilization as a way of decreasing the amount of EtO use and exposure. **Mr. Cogdill** responded that Medtronic is trying to combine products into one cycle and reducing the quantity to get full utilization of the chambers.

Dr. Burr asked what the annual consumption of EtO in tons is for a typical facility as well as the aggregate annual emissions. **Mr. McEvoy** replied that it could vary greatly according to the size of facilities, the number of chambers, and other factors. **Dr. Burr** commented that that would be important data to have.

Michael Yaszemski, M.D., Ph.D., asked what constitutes the abatement process. **Mr. May** replied that his company is using so little ethylene oxide that it can be passed through a cationic resin that converts it into an inert material, leaving no byproduct. **Mr. Christensen** explained that his sterilizers use a heated catalytic bed that has a 99-plus percent efficiency of converting ethylene oxide into water vapor and carbon dioxide.

Chairperson Lewis asked what the barrier is to wider-spread implementation of similar systems. **Mr. Christensen** suggested that sizing up would be an issue. **Mr. McEvoy** acknowledged that that system is used frequently in the European facilities along with a number of other technologies.

Stephen Wilcox, Ph.D., observed that EPA's concern seems to be with emissions and not with the use of EtO. He asked why the focus of the discussion is not on abatement. **Mr. Cogdill** replied that Medtronic uses a lot of the same abatement equipment which is in excess of 99%. He pointed out that Mr. Koerber referred to challenges with fugitive emissions.

Mathew Arduino, Dr.P.H., asked if the current abatement technologies are actually adequate to meet the EPA requirements. He also asked if exhaust air from the aeration process could go through some sort of abatement mechanism as well. **Mr. Christensen** related that in his case, all of the ethylene oxide from the sterilizer goes directly to the abatement system because his process sterilizes and aerates inside the chamber.

Dr. Tung asked Mr. Cogdill if there is a limitation to how far something can be transported once it has been sterilized. **Mr. Cogdill** responded that Medtronic conducts transportation studies and stability testing. He also replied that the company's products are shipped worldwide and that they are acceptable as long as the packages are intact.

OPEN PUBLIC HEARING

Janet Trunzo spoke on behalf of AdvaMed. She emphasized the importance of EtO to the U.S. healthcare system, noting that for many medical devices, it is the only effective method for sterilization. She underscored the necessity of ensuring that alternative methods provide the same sterility assurance level and result in the same device performance as EtO. She stated that reduction efforts will continue until a safe and effective replacement is found, and she advised that any potential solutions will not be quickly or easily achieved.

Lara Simmons spoke on behalf of Medline Industries. She stated that Medline's sterilization facility handles over 16,000 surgical kits per day as well as products from customers. She provided a sample surgical kit and explained that they are typically comprised of disposable items, that they can contain up to 200 different components, and that ethylene oxide is the only compatible modality for them all. She described the company's \$5 million upgrade for emission controls, noting that each of the new layered technologies has the ability to reduce emissions by 99%. She encouraged ongoing collaboration to help the industry, legislators, and communities understand the actual situation, the risks involved, and the time that is required to develop alternatives.

Kimberly Nubel, a community representative from Atlanta, Georgia, told the Panel that the learning issues she had as a child seem to correlate with the neurological impacts of EtO. She stated that her children have severe learning issues, that members of her biological family have died from various illnesses, that there have been 45 cases of cancer in 33 homes in her godmother's neighborhood, and that all of these people lived within 4 miles of the Sterigenics plant. She then highlighted the most publicized cancers from EtO exposure, causes of fugitive emissions, and school locations within a 5-mile radius of the facility.

Clarifying Questions from the Panel

Dr. Wilcox asked if it is correct to assume that the systems Medline has in place would meet the issue that EPA has with emissions. **Ms. Simmons** explained that the actual emissions are based on modeling because the technology cannot measure low enough to determine if the risk factor of 0.1 parts per trillion has been reached. She emphasized that the IRIS risk assessment is not a regulatory standard and that Medline is compliant with its current EPA permit.

Carol Pekar, M.B.A., RAC, Industry Representative, asked Ms. Simmons and Ms. Trunzo what would be involved in getting FDA approval for an alternate method of sterilization. **Ms. Simmons** replied that the validation process as well as material compatibility and shelf-life studies would take years to complete. She added that switching from one method to another is also very time consuming. **Ms. Trunzo** remarked that the

quantity of years would be difficult to estimate because of the number of steps involved.

Isaac Benowitz, M.D., asked Ms. Nubel why the community group chose a 5-mile radius as its focus for potential impacts. **Ms. Nubel** replied that it was chosen based off of what news media outlets were reporting.

ELIMINATION OF ETHYLENE OXIDE EMISSIONS FOR MEDICAL DEVICE STERILIZATION: MODALITIES WITH EXISTING INDUSTRIAL INFRASTRUCTURE

Gamma Sterilization of Medical Devices

Emily Craven, a radiation processing technology professional at Mevex, provided a synopsis of the gamma sterilization process. She noted that radiation can alter the polymers that make up most single-use medical devices, and she stressed the importance of knowing how these materials and their properties can be affected. She reviewed the methods that are used in making dose determinations, noting that the method chosen is typically based upon product requirements, manufacturing controls, and the selected radiation process. She then discussed maximum allowed dose/material compatibility, radiation as an alternative to ethylene oxide, regulation of gamma sterilization, and gamma capacity constraints. She acknowledged that there is currently no solution that would allow the transfer of a significant volume of EtO-sterilized devices to gamma, and for many products, ethylene oxide is still the best process available.

X-ray and E-Beam Based Industrial Sterilization Methods

Thomas Kroc, Ph.D., a physicist at the Fermi National Accelerator Laboratory, gave an overview of x-ray and electron beams and the ways in which they differ from gamma. He discussed the types of devices that can be sterilized with these methods, described the required infrastructure, and compared the energy spectra of all three modalities. He then touched on the potential of accelerator technology in this area, looked at the ways that it can be done, and presented capacity comparisons. He pointed out that because of the shorter radiation times with e-beam and x-ray, the detrimental processes caused by oxidative effects will be less prevalent.

Moist and Dry Heat Sterilization of Medical Devices

Jonathan Wilder, Ph.D., Quality Processing Resource Group, LLC, identified reliability, cost effectiveness, and excellent product penetration as the reasons why EtO is typically used to sterilize medical devices. He presented a compilation of materials that are usually sterilized in ethylene oxide and subsets that are less compatible with radiation, steam, and dry heat. After looking at potential alternate sterilization methods for these materials, he then compared thermal sterilization to ethylene oxide and steam to dry heat. He related that there are a large number of polymers that can be migrated to thermal sterilization methods, that the details of specific device construction may constrain this migration, and that changing the production model will be costly. He concluded that some

materials currently sterilized with EtO cannot be migrated to radiation sterilization nor to steam or dry heat; the effects of high-temperature sterilization can make migration of otherwise compatible devices impossible; and that because the logistics and equipment for thermal sterilization are so different from EtO, it would take a lot of capital and time to implement.

Clarifying Questions from the Panel

Chairperson Lewis asked if the levels of radiation are sufficiently high enough to penetrate steel in medical devices or implants. **Ms. Craven** replied that currently all metal components are being sterilized with photon-based radiations such as gamma and x-ray because they are very penetrating. She stated that there are no issues with absorption or blocked radiation.

Stephen Li, Ph.D., asked what would be the driving force behind making a decision to switch from ethylene oxide to gamma, x-ray, or thermal. **Ms. Craven** replied that there is currently a big push from companies to have the ability to move from one type of modality to another, partly because of the challenges with ethylene oxide.

Mr. Socola asked how long it takes to build new gamma facilities. **Ms. Craven** replied that the licensing process and building of the infrastructure usually takes a year.

Dr. Kim asked if gamma radiation facilities have additional capacity to take on more. **Ms. Craven** replied that presently they do not because of the amount of additional pressure on gamma supply.

Dr. Arduino asked if radiation sterilization can be used on electronic components. **Ms. Craven** replied that they are usually not radiation compatible.

OPEN PUBLIC HEARING

Chau Powell spoke on behalf of Premier, Inc. He gave an overview of proactive steps taken by the company to identify and mitigate the potential impact of sterilization facility closures. These steps include the creation of a product disruptions team, assessment of potential downstream risk, and quantification of the availability of excess sterilization capacity in the United States. He reported that capacity is nearly exhausted and would be exceeded by the closure of two more facilities.

He then made the following recommendations:

- Visibility to upstream stakeholders in the supply chain must be created.
- Successful drug shortage solutions should be applied to medical devices.
- A collaborative approach should be taken in balancing the risks associated with current techniques and patient care needs.

Sam Ajizian, M.D., spoke on behalf of Medtronic. He identified various sterilization techniques used by the company and acknowledged that no perfect method exists. He stated that EtO continues to be the most widely used gaseous sterilization agent in the world, and for many products, it is the only validated method to ensure sterility without affecting the integrity and function of devices over their lifespan. He stated that the

company is engaged in evaluating possible processes and technologies to further reduce ethylene oxide usage and emissions and will continue working collaboratively with all stakeholders. He cautioned against abruptly banning or restricting the use of EtO, asserting that it must continue to be available to ensure the safety of medical devices and to avoid shortages.

Josh Babb spoke on behalf of the Health Industry Distributors Association. He noted that ethylene oxide is used because many products cannot tolerate other sterilization procedures, that more than 50% of all medical devices are sterilized using EtO, and that there are no viable alternatives currently available to replace it. He emphasized the importance of understanding that a disruption at a single facility could have a magnified impact across the entire country and in every healthcare setting, and he called for thoughtful consideration of these consequences. He urged caution and collaboration among all industry partners in ensuring that the healthcare supply chain will continue providing safe products for patients.

Danielle Walsh, M.D., FACS, spoke on behalf of the Society of American Gastrointestinal and Endoscopic Surgeons. She encouraged the continuation of exceptionally high standards for all sterilization processes and rigorous assessment of alternative methods. She insisted that efforts to increase the safety of ethylene oxide must be initiated with guaranteed access to essential and critical devices.

Clarifying Questions from the Panel

Chairperson Lewis asked Mr. Powell and Dr. Ajizian for comment on how the industry might be responding to mitigation strategies relative to the use of ethylene oxide and what the time frame may be for adopting them. **Dr. Ajizian** replied that Medtronic's position is one of responsible use of EtO. He pointed out that even with the proposed changes, the company would have to work with its sterilization partners and internal experts to ensure that products would not be compromised in any way. **Mr. Powell** stated that the primary point to consider is how quickly a solution can be created that will be sustainable over the long term. He said that he believes the industry is taking these concerns very seriously.

Lynn R. Goldman, M.D., M.S., M.P.H., observed that this is not a new issue and that she has not heard anything about what steps are being taken to transition to a different way of doing business. **Dr. Ajizian** pointed out that one of the differences now is that companies are participating in FDA's innovation challenge, that there is tangible work being done by multiple stakeholders to decrease EtO input and to increase recovery, and that it is not an overnight process. He maintained that ethylene oxide, when used responsibly, is safe and effective and meets the need for having sterile, safe, and available devices. **Mr. Babb** replied that distributors are looking at the constraints that have been posed on both supply and demand, and he pointed out that the supply chain has many other demands placed on it beyond sterilization needs. He emphasized that it cannot take a brisk or agile shift in another direction at this time.

Teresa Wells, RN, B.S.N., M.B.A., asked if the facilities have plans for other kinds

of serious events such as economic or weather-related crises. **Mr. Babb** replied that HIDA has been working closely with the federal government in an effort to be more proactive in protecting the supply chain from natural vulnerabilities.

Dr. Li asked why there is not a more aggressive plan to expand capacity.

Mr. Powell suggested that companies are unsure whether investing millions of dollars into increasing capacity will be feasible if they are going to be shut down anyway.

PANEL DELIBERATIONS/FDA QUESTIONS

Dr. Ortega read Question 1: If EtO sterilization is reduced, eliminated or replaced to a different sterilization modality, how can the impact to healthcare delivery organizations be minimized?

Sandra Myers, D.N.P., explained how the Veterans Administration reduced the use of EtO in its facilities by 80%. She recommended a segmented contingency plan starting at the hospital facility level.

Ms. Pekar stated that industry needs incentives and that less conservative approaches should be considered.

Dr. Goldman commended FDA's efforts in motivating industry to devise new technological approaches and in helping to accelerate the R&D process.

Dr. Li pointed out that the Panel does not know what the alternative processes are. He further noted that unless the replacement technology has outcomes similar to EtO, from all practical standpoints, its impact will be negative.

Suzanne Schwartz, M.D., Acting Director, Office of Strategic Partnerships and Technology Innovation, noted that the Agency is seeking guidance on what can be done to prevent further disruption within the supply chain if the current situation were to continue.

Chairperson Lewis asked if there is a way to encourage industry to quicken its efforts in reducing ethylene oxide exposure to the public and in developing alternate procedures. **Dr. Schwartz** replied that FDA intends to continue working with stakeholders to determine if there are other potential incentives to bring about possible mitigations.

David Krause, Ph.D., Deputy Office Director, Office of Health Technology 4, Surgical and Infection Control Devices, brought up additional points of consideration such as other methods of sterilization, ways of reducing emissions, and quicker review processes.

Dr. Tung mentioned that there have been a number of significant drug shortages that were handled in a satisfactory manner. He asked if these occurrences are viewed differently from what would happen if sterilization plants are shut down. **Dr. Schwartz** explained that FDA has certain elements of authority with drugs regarding communication and transparency issues that it does not have with devices.

Chairperson Lewis suggested that the feedback loop on the local level during a worst-case scenario, as well as the public reaction to it, would have greater potential than what FDA would do.

Dr. Burr suggested looking at the situation from two time frames: what can be done now and what will be beneficial in future years. He emphasized that there is no reason why existing abatement technologies would not bring these plants within EPA standards in a short period of time.

Dr. Schwartz explained that FDA's innovation challenges are focused on short and long-term solutions and that abatement issues do not fall under its purview.

Ashley Faulx, M.D., pointed out that too many items are being sterilized that do not need to be sterile. She suggested that identifying and rooting out these items could help in reducing the volume that goes into sterilizers.

Michael A. Saubolle, Ph.D., emphasized the importance of prioritizing what needs to be done and of working in partnership with state health departments.

Dr. Goldman suggested having a risk framework and encouraged collaboration between FDA, the EPA, and state government officials.

Chairperson Lewis noted that one potential area is to look at requirements to see where reductions can be made. He remarked that the Panel would most likely not be able to deal with the specifics of this issue.

Dr. Ortega read Question 2: What can FDA do to help mitigate and prevent device shortages due to reduced device sterilization capabilities?

Ms. Pekar suggested that companies be advised that overkill may not always be needed. She also proposed sample validation protocols, special 510(k) status, and quick reviews.

Mr. Socola recommended doing a risk assessment.

Charity J. Morgan, Ph.D., suggested that fast-tracking certain devices may be helpful.

Dr. Ortega read Question 3: Can changing EtO sterilization cycles or sterilization loads reduce EtO use while maintaining effective sterilization? Can the Panel provide a recommendation for which methods appear to be the most promising?

Keziah (Kate) Sully, M.D., Consumer Representative, suggested that it may be of benefit to find out what materials can yield a lower ppm.

Ms. Wells endorsed EtO sterilization of products that absolutely need it and of weeding others out, particularly expendable items included in surgical packs.

Dr. Kim encouraged continued efforts to decrease concentrations.

Dr. Li observed that there is a financial incentive for companies to improve their processes and that they should already be doing these things.

Chairperson Lewis advised that the Panel is not able to determine what strategies would work better than others, but it does recommend forward momentum in finding useful solutions as quickly as possible.

Dr. Ortega read Question 4: Can new or different methods of validating EtO sterilization cycles potentially result in a reduction of EtO use while still maintaining an effective sterilization process? If so, how?

Ms. Wells suggested a standardized process to categorize items for different methods of sterilization.

Ms. Pekar proposed recommendation to companies of the BI/bioburden validation

method.

Dr. Ortega read Question 5: Should sterilization of some medical devices to a less rigorous sterility assurance level (e.g. 10^{-5} , 10^{-4} , instead of 10^{-6}) be considered as part of the approach to reduce sterilant use? How do you see this changing the patient risk profile for sterile devices if a different sterility assurance level is determined to be acceptable?

Chairperson Lewis stated that reducing or increasing the patient risk profile is not acceptable. He also noted that the Panel's position is that the standards are higher than they need to be given the manner in which they are being executed.

Dr. Ortega read Question 6: Are there large-scale industrial sterilization modalities that can take over a portion of the EtO sterilization performed for medical devices in the short or long term? If so, can the Panel provide a discussion of the path forward for these modalities? And if not, what are the barriers and challenges preventing wider utilization of these modalities?

Dr. Li stated that it depends on the device and what it is made of. He pointed out that in most cases the device itself dictates the method of sterilization.

Chairperson Lewis suggested that there are probably more devices that can be sterilized in multiple ways than what is believed, and there are opportunities for other modalities to be utilized.

Dr. Goldman remarked that more EtO facilities could be built and that the existing ones could be scaled up, but nobody is doing it.

Chairperson Lewis commented that there are opportunities, but they would require detailed evaluations of each device.

Dr. Wilcox stated that EtO use needs to go up, not down, that the problem is with emissions, and that the emission problem is solvable. He further stated that it should be made clear that the Panel is not assuming that the use of EtO is going to cease, but it is considering what should be done if it happens.

Chairperson Lewis agreed. He acknowledged that abatement procedures and techniques are readily available and could be implemented. He went on to say that FDA should take a role in investigating how agencies and the private sector can be encouraged to move in that direction.

Dr. Schwartz noted that the Agency's main focus has to be on decreasing EtO emissions due to public sentiment and concern across communities.

Dr. Kim observed that gamma radiation seems to be the only large-scale alternative and that it also has its own challenges.

Dr. Li pointed out that the Panel has not heard a lot of detail about abatement, that he believes it can be improved, and that currently there are no alternative solutions.

Dr. Benowitz asked what has been done to determine whether gamma radiation might be an available option for other devices.

Dr. Li explained that gamma radiation is more effective and efficient for certain devices, and there are very few on which both methods can be used.

ADJOURNMENT

Commander Garcia made general announcements concerning the next day's meeting.

Chairperson Lewis then adjourned the meeting at 5:38 p.m.

Summary Prepared by

Karen D. Martini
Free State Reporting, Inc.
1378 Cape St. Claire Road
Annapolis, MD 21409
(410) 974-0947
November 16, 2019