SUMMARY MINUTES

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

GENERAL HOSPITAL AND PERSONAL USE DEVICES PANEL

November 7, 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 Physiatrist
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 8:00 a.m.

INTRODUCTION OF THE COMMITTEE

Chairman Lewis asked the panel members and the FDA staff to introduce themselves, after which he noted the presence of a quorum and stated that the Panel members had received training in FDA device law and regulations.

CONFLICT OF INTEREST STATEMENT

Patricio Garcia, M.P.H., CDR, USPHS, Designated Federal Officer, read the Conflict of Interest Statement and stated that the Panel would discuss and make recommendations on industrial ethylene oxide sterilization of medical devices and its role in maintaining public health, as well as the risk of infection presented by reprocessed duodenoscopes.

He reported that no conflict of interest waivers had been issued.

He then introduced Ms. Carol Pekar as the Industry Representative and noted that invited speakers Dr. Michelle Alfa and Cori Ofstead had acknowledged interests with affected firms.

DAY 1 SUMMARY AND OVERVIEW OF DAY 2

Clarence Murray, III, Ph.D., Surgical and Infection Control Devices, gave a brief summary of the previous day's presentations and an overview of the remaining agenda.

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

Hydrogen Peroxide

Sylvie Dufresne, Ph.D., IM3 Consulting Group, described the process of hydrogen peroxide sterilization and industrial sterilization of medical devices. Since H_2O_2 is conducted in a vacuum, the devices need to be able to withstand a vacuum of 1 torr or below. The process is a delicate balance of temperature and pressure in order to keep the H_2O_2 in a vapor form in order to penetrate the product. While it may oxidize on natural rubber and cellulosic material, hydrogen peroxide has good compatibility with most medical devices, at least for one or two cycles. She pointed out that AAMI TIR 17 that has a good list of all materials compatible with hydrogen peroxide and other sterilization processes. On the down side, H_2O_2 cannot pass through non-porous materials such as aluminum pouches

used for packaging and was not compatible with cellulosic materials such as cardboard. Tyvek, she said, is a good packaging choice for this process. Even after ventilation, porous materials will have some H_2O_2 residual; however, it is at a very low level and posed no threat to humans. She concluded that hydrogen peroxide sterilization could be an alternative to EtO for many specific devices packaged using Tyvek that do not have really small lumens, such as cardiac catheters.

Nitrogen Dioxide

David Opie, Ph.D., Noxilizer, Inc., discussed nitrogen dioxide sterilization as a possible replacement for ethylene oxide. He said in the NO_2 sterilization process, nitric oxide or NO combines with nitrogen dioxide to form N_2O_3, which reacts with guanine and cytosine, irreversibly damaging DNA and RNA. NO_2 sterilization is performed in a vacuum, generally about 20 torr or 26 mbar. The process has very broad material compatibility, with exceptions being cellulose and Delrin. NO_2 is a surface sterilant that does not penetrate materials, such as a needle shield on a syringe or a stopper on a vial. Currently, capacity for NO_2 sterilization is small, only about 800 pallets a year in 2020, but is expected to grow to at least 7,500 pallets in 2021. NO_2 sterilization could easily be installed in-house at the point of packaging. It is not explosive, and operator exposure studies demonstrated no exposures greater than 0.1 ppm. Shorter cycle times would allow smaller chambers to match the throughput of large ethylene oxide chambers, and every load processed relieves the capacity of EtO sterilization and thereby reduces ethylene oxide emissions.

Chlorine Dioxide

Paul Lorcheim, P.E., ClorDiSys Solutions, discussed chlorine dioxide sterilization. Chlorine dioxide is able to be accurately measured and monitored with a UV-vis spectrophotometer, and therefore, the process is able to be very tightly controlled. Unlike chlorine, which reacts with water to form chlorous acid, chlorine dioxide maintains a neutral pH in water. ClorDiSys primarily uses chlorine dioxide to temporarily sterilize an area or a building, such as a food facility. When the building is vented, the sterility is broken. Like other methods, chlorine dioxide will penetrate Tyvek, and its very small molecules are able to get into very small areas and surround target organisms. Sterilization is done at ambient pressures, and dose accumulation is easily monitored so the cycle is not stopped until the desired dose is reached. Commonly used on fruits and vegetables as well in treatment of drinking water, the process leaves no measurable residues. Non-explosive and noncarcinogenic, chlorine dioxide sterilization is compatible with electronics and batteries. Like other methods, it does not penetrate cellulosic materials. Not currently widely used for medical devices, it is however used on human bones and tissues as well as temperature-sensitive products. He concluded that the process is very scalable and, apart from cardboard packaging, could be a promising replacement for EtO sterilization.

Vaporized Peracetic Acid and Other Chemicals

Joe McDonald, Ph.D., Cantel Medical Corp., discussed the pros and cons of medical

device sterilization using vaporized peracetic acid, which he explained is an effective antimicrobial agent used for decades in the food and medical industry as a disinfectant. The chemical is injected into a vacuum chamber where it is maintained in vapor state to accomplish sterilization. After ventilation, a filtration system traps the sterilant, breaking it down into harmless water, carbon dioxide, and oxygen. While the company is currently focused on in-line, in-house sterilization, Dr. McDonald said he felt comfortable they would be able to scale up to larger chambers. Like other methods, cardboard packaging is a barrier; however, it is able to penetrate Tyvek. Peracetic acid has very good material compatibility, especially with electronics and batteries.

Healthcare Sterilization of Medical Devices

Susan Klacik spoke on behalf of the International Association of Healthcare Central Service Materiel Management (IAHCSMM) on the possibility of healthcare facilities performing industrial sterilization of ethylene oxide. She outlined numerous challenges faced by hospital sterile processing departments, which are hectic areas with constant interruptions. Packaging is done manually. Loads are not standardized. Indicators have to be placed in each and every package. Hospital space is limited, so enlarging these facilities is not practicable. Due to proximity to surgery, increased capacity would increase traffic and interfere with patient transport. EtO sterilization would require a dedicated exhaust as well as environmental monitoring would be required and engineering controls to reduce emissions. Hospitals would need increased funding for additional technicians. Hospitals are currently struggling to cut down on unnecessary processing by turning to an increasing number of disposable products. All of the medical supplies would need to be revalidated, incurring still more cost. For all of these reasons, she said, bringing single-use disposable products to be sterilized in-hospital is not a viable solution.

Clarifying Questions from the Panel

Chairman Lewis commented that current use of peracetic acid seemed to be limited to small-volume applications, and he wondered what obstacles or drawbacks there might be in scaling it up for industrial use. **Dr. McDonald** explained that it would be possible to scale to a larger operation, and he pointed out that due to shorter cycle times, even smaller operations could process significantly more items.

Chairman Lewis asked what sort of timeline would be required to achieve the volume of a quarter of a million pallets in each of the four modalities in order to replace the current volume of ethylene oxide sterilization in the United States. **Dr. Opie, Dr. McDonald,** and **Mr. Lorcheim** agreed it would take roughly a decade.

Carol Pekar, M.B.A., RAC, Industry Representative, asked whether peracetic acid could penetrate cellulosic material such as cardboard. **Dr. McDonald** replied that it could not. **Ms. Pekar** commented that since all four methods had the same drawback, perhaps the packaging needed to be changed.

Avery Tung, M.D., asked about the environmental impact of nitrogen dioxide as it leaves the sterilization facility. **Dr. Opie** explained that the scrubbing process removed all but 1 ppm or less of nitrous oxide from the exhaust stream, as detected by sensors.

Keziah (Kate) Sully, M.D., Consumer Representative, asked about occupational or environmental considerations for waste as a result of hydrogen peroxide sterilization. **Dr. Dufresne** explained that since the chamber is under vacuum, any leaks during the process would remain in the chamber and that catalysts are used to destroy hydrogen peroxide during ventilation afterwards.

Chairman Lewis asked each presenter whether their process would be more or less expensive or the same cost as ethylene oxide sterilization. **Mr. Lorcheim** replied that it would probably be equal or less expensive. **Dr. Opie** and **Dr. McDonald** felt it would be a similar expense. **Dr. Dufresne** deferred to industry regarding hydrogen peroxide.

Michael A. Saubolle, Ph.D. asked what it would take for healthcare facilities to replace their ethylene oxide sterilization processes completely over the next few years. **Ms. Klacik** pointed out that all of the medical devices would have to be validated for the change in sterilization modality, which combined with material compatibility issues and space requirements would make it very difficult.

Dr. Saubolle then asked whether hospitals would be willing to go through their devices and determine which ones could be sterilized without ethylene oxide.

Teresa Wells, RN, B.S.N., M.B.A. volunteered that the VA has been working to remove EtO since 2005, and currently only 20% of products still required EtO sterilization, and she believed only duodenoscopes could not be converted to another modality.

Suzanne Schwartz, M.D., Acting Director, Office of Strategic Partnerships and Technology Innovation, reminded that they should be focusing on terminal sterilization of single-use devices.

Chairman Lewis asked about the capacity for hospitals to assume in-house sterilization of products currently undergoing industrial sterilization. **Ms. Klacik** replied that hospitals do not have the space, personnel, or logistics to assume those functions.

Robert E. Burr, M.D., M.Sc., inquired whether current chambers could be retrofitted for different modalities. **Mr. Lorcheim** answered that standard steam autoclaves or ethylene oxide chambers are very easily converted to chlorine dioxide. **Dr. Dufresne** pointed out that injection methods were different and there might need to be some adaptation. **Dr. Opie** said that while new steam autoclaves were easily modified for use with nitrogen dioxide, retrofitting used ones could have unintended consequences.

PANEL DELIBERATIONS/FDA QUESTIONS

Ryan Ortega, Ph.D., Surgical and Infection Control Devices, read Question 7: Are there alternative sterilization methods being developed that can take the place of EtO sterilization processes with respect to scalability and material compatibility? And 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 large-scale industrial utilization of these modalities?

Gary Socola pointed out that there are no standards or guidance documents for alternative sterilization processes, and manufacturers would be at risk for lawsuits. Combined with the fact that some of these single-use products have a 5-year shelf life, he felt it would take perhaps several decades to replace EtO with alternative modalities.

Sandra Myers, D.N.P., wondered whether the new facilities would also be

unpopular in surrounding communities.

Eugene S. Kim, M.D., brought up the material incompatibility with cardboard packaging, and he suggested sterilization might need to be done during the manufacturing process instead of afterwards.

Stephen Li, Ph.D., stated that the onus seemed to be on the manufacturers to change sterilization methods, whether by choice or necessity, and he recommended that the FDA not be tempted to lower their standards for sterility acceptance because of the extreme need.

Dr. Burr inquired whether any trials had been conducted in order to reach the current validation standards.

Steven Elliott, M.Sc., Surgical and Infection Control Devices, explained that sterility assurance level calculations were developed using a percentage-based approach.

Ms. Wells asked whether new filtration technologies could be used to reduce EtO emissions to undetectable levels.

David Krause, Ph.D., Deputy Office Director, Office of Health Technology 4, Surgical and Infection Control Devices, asked the Panel to focus on the first part of the question, which was what the path forward might be for these alternative modalities.

Chairman Lewis pointed out that the modalities under discussion had significant promise but also significant drawbacks, the most important being the inability to penetrate cardboard. The path forward, therefore, would necessarily be very slow.

Mr. Socola recommended that a request be forwarded to AAMI for a working group to review a national standard for alternative methodology for industrial sterilization.

Dr. Saubolle stated that he felt the requirements for moving forward were reduced regulatory uncertainty, a template for material change, and a validation template.

Dr. Schwartz asked whether the Panel believed that FDA should be pursuing methods of removing regulatory uncertainty, even for niche-related categories, recognizing the lack of immediate scalability. **Dr. Saubolle** replied in the affirmative. **Chairman Lewis** said he felt the entire Panel would agree.

Isaac Benowitz, M.D., asked whether FDA has considered an innovation challenge to define broad categories of materials and types of devices compatible with alternative sterilization methods. **Ms. Pekar** suggested an innovation challenge to replace cardboard packaging.

Dr. Ortega read Question 8: How can FDA help implement adoption of these EtO reduction or EtO replacement strategies and facilitate reduction of EtO emissions within our regulatory framework?

Chairman Lewis commented that he felt the question had already been answered and asked if any of the Panelists had anything to add. There was no response.

Dr. Ortega read Question 9: Can the Panel identify devices or device types that would be difficult to sterilize without using EtO that may be amenable to the application of alternative sterilization modalities?

Dr. Saubolle commented that the biggest issue seemed to be the packaging.

Chairman Lewis pointed out that non-packaging related issues are devices with

long, narrow channels and with materials or liquids within a closed container.

Dr. Li stated that if the sterilization method affects the properties of the device material, then the packaging issue was irrelevant; therefore, that was of primary concern to him. Also, changes in the material could be so subtle as to not be noticeable right away; therefore, he did not feel confident that any devices could be identified for a particular sterilization modality without significant testing.

Michael Yaszemski, M.D., Ph.D., added that devices sometimes contained combinations of materials that were not immediately obvious.

Mr. Socola recommended that FDA look carefully at self-injectable, mechanical devices and syringes as they would be particularly difficult to both sterilize and validate due to their complicated packaging systems.

Dr. Ortega read Question 10: Does the Panel have any other recommendations for reducing EtO risk without causing medical device shortages?

Dr. Sully asked about the possibility of importing devices sterilized with EtO from outside the U.S. **Dr. Krause** acknowledged that while such devices are imported, other countries would eventually have the same issues with ethylene oxide.

Dr. Burr pointed out that the data on EtO emissions was not very strong, and it was not clear that there was a significant problem in a well-engineered, well-run plant. Therefore, plants simply need to apply and maintain the proper technology.

Dr. Yaszemski agreed and stated that it was likely that plants that had been shut down were not applying the technology correctly.

Ms. Pekar stated that an attempt should be made to reduce EtO usage, and perhaps validations could be done across device types, for simplification. She added that anything FDA could do to reduce regulatory uncertainty, provide incentives, accelerated reviews, and validation templates would be helpful.

Dr. Kim asked whether there is any standardization being used in scrubbing emissions, and he said that the process should be standardized and monitored.

Debra Dunn, Patient Representative, related that she lived near the Willowbrook facility, and she understood the company had reduced emissions to very acceptable levels, but the Governor of Illinois had stepped in and closed the plant due to public outcry.

Stephen Wilcox, Ph.D., suggested that there was nothing to be lost by encouraging these new technologies since added capacity was welcome even if EtO is not restricted.

Chairman Lewis suggested the question had been covered extensively.

REDUCING THE RISK OF INFECTIONS FROM REPROCESSED DUODENOSCOPES

FDA PRESENTATION

Shani Haugen, Ph.D., Gastroenterology and Endoscopy Devices, introduced the subject of the second half of the day. She began with a brief background around the clinical use of duodenoscopes in endoscopic retrograde cholangiopancreatography (ECRP), followed by FDA's actions to address risk of infection from reprocessed scopes. In February 2015

FDA issued a Safety Communication advising the public of a series of outbreaks that had been occurring starting in 2013 related to poorly processed duodenoscopes. In May of 2015, FDA convened an Advisory Committee to discuss the issue and hear from experts and facilities on reducing the risk of infection for patients. In July 2015, March 2016, and May of 2019, FDA participated in CDC's Healthcare Infection Control Practices Advisory Committee meeting (HICPAC), to provide updates and gain feedback from infection control experts.

During this time, FDA has worked with manufacturers to update and validate reprocessing instructions to include additional cleaning steps as areas of concern were identified. FDA has also worked with manufacturers to improve product design, to increase accessibility and reduce contamination. In August of 2015, FDA released a summary of supplemental measures to enhance duodenoscope reprocessing that emerged from the May 2015 Advisory Committee meeting, including microbiological culturing, ethylene oxide sterilization, use of a liquid chemical sterilant processing system, and repeat high-level disinfection. In 2015 FDA conducted directed inspections and issued warning letters to the three U.S. duodenoscope manufacturers for various violations. And in October 2015, recognizing the need for additional real-world data on use of duodenoscopes, FDA ordered duodenoscope manufacturers to conduct postmarket 522 surveillance studies.

Dr. Haugen presented a slide showing a graph of Medical Device Reports (MDRs) associated with infection, patient exposure, or device contamination from January 1, 2015 to July 1, 2019. The graph illustrated a dramatic increase in reporting of device contamination since 2015, likely due to increased sampling and culturing. There has also been a decrease in the number of reported infections since 2015; however, the continued reports of infections reflect the need to improve the safety of reprocessed duodenoscopes.

Results from human factors studies indicate that reprocessing instructions in current user manuals are difficult for reprocessing staff to comprehend and follow. Many reprocessing staff missed one or more steps in the process and needed additional training, and the descriptions of some of the processing steps in the user manuals were unclear.

Dr. Haugen stated that while not every exposure to a contaminated scope leads to infection, these rates are concerning to FDA and illustrate that improvements are necessary. She went on to outline the questions that the FDA would be asking the Panel. Then she discussed two new duodenoscope designs cleared in 2017 that featured disposable endcaps, which address a particular area of concern for reprocessing. In presenting a high-level overview of duodenoscope reprocessing, she noted that the discussion was no longer around industrial sterilization but small-scale ethylene oxide sterilization in a healthcare facility.

Finally, she discussed a handful of presentations featuring surveys of healthcare facilities using duodenoscopes that indicate that as much as 5% of reprocessed duodenoscopes remain contaminated. She discussed FDA's definition of high-level disinfection versus sterilization and sterility assurance levels and concluded by saying that FDA is concerned that current practices for reprocessing duodenoscopes are not sufficient to avoid all infections associated with their use, and FDA was therefore seeking the Panel's input on next steps.

Clarifying Questions from the Panel

Dr. Wilcox wondered why duodenoscopes were not disposable given the current technology. **Dr. Haugen** replied that while disposable duodenoscopes are in development, as of yet, none have been cleared by FDA. She pointed out that one of the FDA questions related to the urgency of transition to disposable devices, and she noted that upcoming speakers would likely comment on challenges associated with switching to disposable duodenoscopes.

Chairman Lewis pointed out that the cost of these devices ranges from $30,000 to $40,000 each, which is another significant obstacle.

Dr. Burr wondered whether there might be identifiable patient factors that increase the likelihood of infection from a contaminated scope. If so, perhaps strategies such as peri-procedural antibiotic administration might reduce the risk in those patients.

Dr. Haugen acknowledged that these patients tend to be sicker in general, and factors like stent delivery and antibiotic use had been looked at, but she suggested that a clinician should address this question.

Chairman Lewis pointed out that a high number of patients undergoing ERCP had severe sepsis, as the primary treatment was intended to unblock the common duct. The overall mortality rate was in the range of 10 to 25%. While there are patients with relatively benign conditions, a significant fraction of patients undergoing ERCP need it as a lifesaving measure.

Lynn R. Goldman, M.D., M.S., M.P.H., noted that there is some information in infectious disease literature regarding risk stratifying patients at higher risk for infection, but the data was not robust. She added that they had looked at doing rectal swabs to identify patients who might be at risk.

Chairman Lewis pointed out that duodenoscopes were usually cleaned by minimum-wage workers that might benefit more from comprehensive hands-on training than complex written instructions, and he asked for comment on how training and monitoring programs might be implemented. **Dr. Haugen** noted that while FDA has a great deal of input on training for Class III high-risk devices, duodenoscope are Class II devices, and therefore, it is not within FDA's purview to regulate training. She added that FDA looked forward to comments on how training might be determined and implemented by professional societies.

Chairman Lewis asked about the selection of the number 250 as a standard for durability testing. **Dr. Haugen** replied that an informal survey was done of roughly 30 facilities to determine the number of uses of a duodenoscope in an average year, and 250 captured 90% of the cases.

James W. Collins, RN, CNOR, asked about the spike in the number of exposures and reports in 2018 and 2019 despite the enhanced measures that were given in endoscope reprocessing. **Dr. Haugen** replied that might be due to increased sampling and culturing done by facilities in response to a recommendation by FDA in August of 2015.

Dr. Saubolle wondered whether the elapsed time between use of a scope and decontamination or cleaning had any relevance. **Dr. Haugen** replied there was some variability in that number.

Dr. Saubolle pointed out that some of the organisms involved in prior outbreaks such as *Klebsiella pneumoniae* are carbapenemase-resistant and produce biofilms. He wondered whether the material used in the scopes is conducive to biofilm production, especially if they sit around for a day or two.

Dr. Haugen answered that the interior of the endoscope channels was generally PTFE or Teflon, and there have been reports of biofilm inside endoscope channels. She added that some of the expert presenters would be able to speak more on biofilm in the scopes.

Jason Dominitz, M.D., emphasized the varying and often burdensome number of steps enumerated in the cleaning process for endoscopes, and he asked for comment on what could be done to improve the process. **Dr. Haugen** responded there had been discussion in the field about standardizing endoscope reprocessing, which might be beneficial towards simplifying the instructions and making them more intuitive. She added that she looked forward to hearing from the Committee on how such a process could be implemented.

Daryle Gardner-Bonneau, Ph.D., pointed out that in addition to the complex instructions, another consideration is the layout of work spaces, from a human factors perspective. He wondered if there was anything FDA could be doing to look at facility requirements for reprocessing in order to reduce human-factors related mistakes.

Ann Ferriter, Associate Director, Office of Health Technology 3, Reproductive, Gastro-Renal, Urological, General Hospital Device and Human Factors, responded that it was outside FDA's authority, but a speaker would be presenting from the Joint Commission who would get more into the subject.

Dr. Kim suggested that one answer might be to require manufacturers to provide training and certification on reprocessing of their devices.

Lisa Gualtieri, Ph.D., Sc.M., wondered about possible correlation between the age and condition of the device and the contamination rates. **Dr. Haugen** responded that she was not aware of any analysis of that type having been done in the postmarket studies.

OPEN PUBLIC HEARING

Erin Kyle, D.N.P., RN, CNOR, NEA-BC, Association of Perioperative Registered Nurses (AORN), and **Catherine Bauer, M.S.N., M.B.A., RN, CGRN, CFER,** Society of Gastroenterology Nurses and Associates (SGNA), urged the FDA to act both decisively and with caution. Showing images of two disassembled duodenoscopes implicated in disease outbreak, they emphasized the need for improved device design and reprocessing instructions. Citing a belief that requiring sterilization of endoscopes would limit patient access, they stated that their societies do not support that measure. However, they would like to see FDA continue to hold manufacturers accountable for evaluating complexity of IFUs and considering human factors in their development. Also, changes related to duodenoscope reprocessing should include a thorough environmental impact.

Jahan Azizi and **Mary Ann Drosnock** spoke on behalf of Healthmark Industries. The use of a flexible borescope for internal inspections of the endoscope, said Ms. Drosnock, would greatly enhance the duodenoscope reprocessing program. She presented slides showing commonly found debris, damage, staining, and residual moisture found in the channels of the devices. Next, Mr. Azizi discussed a new cleaning technology called turbulent fluid flow (TFF), a closed loop system for cleaning verification and microbial surveillance. Using pressurized gas and sterile water, TFF removed adhered contamination much more effectively than the currently used flush-brush-flush method, as

demonstrated by a comparison of average yields, pre and post sampling.

Rebecca Bartles, M.P.H., CIC, FAPIC, and **Jack Brandabur, M.D**, from Providence St. Joseph Healthcare System, spoke from the perspective of a large healthcare organization. They presented a list of strategies they have implemented to reduce contamination risks, noting that more work still needed to be done. Current IFUs, said Ms. Bartles, are insufficient to ensure adequate high-level disinfection of endoscopes. She asked the Panel to make a recommendation that interim guidelines for reliable reprocessing be produced to support hospitals while further 522 studies are underway. Dr. Brandabur then discussed the complexities involved in replacing the system's extensive inventory of duodenoscopes and EUS scopes, emphasizing that these are expensive capital assets.

Sylvia Garcia-Houchins, M.B.A., RN, CIC, discussed the Joint Commission's focus on disinfection and sterilization over the last 10 years and outlined their survey process used in healthcare facilities. She detailed the many challenges that facilities struggle with, such as physical space and design, lack of training and competency, inadequate preventive maintenance, and poor quality monitoring.

GUEST SPEAKER PRESENTATIONS

Michelle Alfa, Ph.D., FCCM, University of Manitoba, discussed challenges and quality assurance for endoscope reprocessing. After briefly outlining the manual cleaning process, she presented some borescope videos exposing accumulated encrustation of simethicone residuals, and she pointed out the difficulty of removing the material since it is insoluble in water as well as alcohol. She pointed out that the duodenoscope lever mechanism is required to be in the 45 degree angle position during cleaning, and she showed how if that one simple step is missed, it can allow microbial survival during reprocessing. Also, only 34% of respondents to a survey of U.S. sites purported to do any monitoring of manual cleaning. Finally, she presented data from a study looking at drying of endoscopes that showed that automated drying is more effective than manual drying. Most effective, however, is the use of channel-purge storage cabinets, which use sterile tubing to flush every channel in an endoscope with HEPA-filtered or medical grade air. In a comparison of duodenoscopes inoculated with a low level of *Pseudomonas aeruginosa* into the channels, the device stored in the channel-purge storage cabinet remained at the same or lower level of organisms, while the device stored in the standard cabinet had an increased level of organisms over 12, 24, and 48 hours. She concluded that endoscopy sites need a mandated quality systems reprocessing program that addresses inadequate cleaning and moisture removal.

Cori L. Ofstead, M.S.P.H., Ofstead and Associates, presented data on 10 studies conducted in 19 healthcare facilities in 11 states on cleaning and reprocessing various types of endoscopes. At the outset, she stated that in the last five studies, her team detected microbes in more than 50% of endoscopes that had been reprocessed with high-level disinfectant and 13% of ureteroscopes that had been sterilized with hydrogen peroxide gas. On visual inspection of the outside of endoscopes with a borescope or magnifying glass,

they find visible defects or debris on 100% of endoscopes in every institution visited. She presented numerous slides depicting various findings of damage, debris, residue, and visible moisture. She went on to emphasize that low-paid, under-educated workers are expected to read and understand hundreds of pages of documents in order to perform their work, and each different device has its own IFUs for reprocessing. Survey results indicate that workers get less than 1 week of training, and 25% reported less than 1 day of training. Workers reported skipping steps and cutting corners in order to save time as they felt pressure from employers to go faster. They were bothered by odors, felt physical pain, and 40% reported being bullied on a daily basis. Proposed solutions were to provide feedback via monitoring and quality management and to improve the IFUs to provide clear, simple text and recommendations of time to be allocated per cycle. Also, detailed checklists should be provided to technicians. She recommended that manufacturers establish core curriculum to be used in high-quality hands-on training programs, along with guidance on preventive maintenance.

PERSPECTIVES FROM STAKEHOLDER PROFESSIONAL SOCIETIES

Michael L. Kochman, M.D., and **Bret T. Petersen, M.D.,** spoke on behalf of the American College of Gastroenterology (ACG), the American Gastroenterological Association (AGA), American Society for Gastrointestinal Endoscopy (ASGE), and the Society for American Gastrointestinal and Endoscopic Surgeons (SAGES). They expressed a concern that prescriptive guidance with singular solutions may limit implementation and thereby restrict access to lifesaving procedures. They recited 10 asks on behalf of their societies regarding implementation of solutions, device reprocessing transitions, pre and postmarket studies, and surveillance, and they praised the FDA's proactive outreach.

Ms. Klacik, IAHSCMM, discussed the need for more technology for checking scopes, cleaning verification tests, drying devices, and cleaning instruments. IAHCSMM does have a certification program implemented in 2017 for reprocessing flexible endoscopes. She hoped that new sterilization modalities would allow duodenoscopes to move from high-level disinfection to sterilization, noting that while cleaning is still the most important factor, sterilization provides a higher level of quality assurance. She discussed pros and cons of various options, including disposable endcaps and disposable scopes, and she said that time needed for reprocessing should be included in the IFU so that customers understood exactly how much time was required. Finally, she encouraged manufacturers to develop less complicated devices that could be easily disassembled for cleaning, with materials and designs that could undergo steam sterilization, and to provide education and training on the processes.

Michael Anne Preas, M.S., RN, CIC, FAPIC, spoke on behalf of the Association for Professionals in Infection Control and Epidemiology (APIC), the Infectious Diseases Society of America (IDSA), and the Society for Healthcare Epidemiology of America (SHEA). Citing 25 molecularly linked outbreaks despite staff following processes properly, no evidence of damage to the devices or human error, she stated that current interventions were not enough. Lead time is required, but the ultimate goal should be either sterilization

or single-use devices. Manufacturers should be given a hard deadline of January 2021, after which reusable duodenoscopes that cannot be sterilized must be removed from the market. Also, low-temperature sterilization methods should be studied and validated, as ethylene oxide is not feasible for a majority of facilities for a number of reasons, including limited supply, lengthy turnaround times, regulatory barriers, and damage to the devices.

PERSPECTIVES FROM DEVICE MANUFACTURERS

Randy Vader, FUJIFILM Medical Systems U.S.A., introduced the company's newly designed ED-580XT duodenoscope, which features a removable, single-use distal endcap, allowing for direct brush access to the scope elevator mechanism and surrounding recessed distal tip surfaces. He stated that Quick Reference Guides will be provided with the new device as well as enlarged 3D device training models to increase user understanding and adherence to manual cleaning recommendations. Following the rollout of the new device, FUJIFILM will be conducting a postmarket sampling and culturing study in which hopefully the Panel would encourage hospital participation. As for current reprocessing of duodenoscopes, the company recommends manual cleaning and high-level disinfection or 100% ethylene oxide gas sterilization with 12 hours aeration before subsequent patient use. He further recommended certification of reprocessing technicians by accredited training programs.

Ross Segan, M.D., M.B.A., FACS, Olympus Corporation, announced the launch of the Olympus Care Program, which will incorporate training seminars, monthly webinars, and on-demand web-based training in reprocessing their duodenoscopes. The company plans to host more than 25 seminars over the next 12 months throughout the country, which will include live demonstrations along with hands-on training. Additionally, a team of 80 endoscopy specialists are available throughout the country to provide reinforcing training and on-the-spot help at customer locations. Further, Olympus' buyback programs offer customers $10,000 cash or credit to upgrade to the latest technologies. While Olympus duodenoscopes are currently indicated and validated for sterilization through EtO, the company is exploring non-EtO sterilization methods and the utility of offering sterilization services.

J. Hudson Garrett Jr., Ph.D., M.S.N., M.P.H., FNAP, PENTAX Medical, discussed the company's experiences with the 522 study and introduced two new devices, the already cleared ED34-i10T and a second device that is currently seeking clearance. Some of the findings he discussed were human factors in reprocessing, third-party repair, non-OEM-validated cleaning brushes, improper AER use, environmental contamination during sampling, and lack of communication. PENTAX's commitment, he said, is improving clinical outcomes, reducing cost, and improving the overall patient experience of care through device design, competency training and certification, collaboration, and standardization.

Patrick Hurley, Ph.D., Ambu, Inc., discussed the Spaulding system of device classification, focusing specifically on critical and semi-critical devices. While most tools

used with duodenoscopes in ERCP are classified as critical, he said, the duodenoscopes themselves are not. However, critical instruments can come into contact with tissues that then leave deposits in parts of the scope, such as the working channel, the elevator, and the biopsy port. This could be rectified by reclassifying the scopes as critical. Ambu believes single-use endoscopy is a viable solution to eliminate reprocessing concerns and reduce contamination rates on endoscopes. The company is therefore working hard to launch a sterile, single-use duodenoscope in the U.S. in 2020. Dr. Hurley went on to discuss the company's success with single-use bronchoscopes and videoscopes in pulmonology, which he said illustrates that the concept is viable.

Brian J. Dunkin, M.D., Boston Scientific Corporation, stressed the importance of pursuing the technology of single-use duodenoscopes. As the world's largest manufacturer of single-use scopes, Boston Scientific is also pursuing development of a single use duodenoscope that will meet the requirement of being equivalent to its predicate device already on the market. Costs, he said, should be weighed against costs of maintaining a large inventory to ensure throughput, compliance training of personnel for reprocessing the devices, and the cost to patients of developing an endoscope-acquired infection. Boston Scientific also plans to sponsor an environmentally sound recycling program for the single-use devices.

Clarifying Questions from the Panel

Dr. Myers asked whether FUJIFILM's Quick Reference Guide included an estimate of the time necessary to perform each procedure. **Mr. Vader** introduced his technical expert, **Keith Nelson**, Director of Infection Control, who replied that the guides did not specify times.

Dr. Goldman requested more information about the recycling program. **Dr. Dunkin** explained that the scopes would be recycled down to their component elements, which would then be recycled responsibly and not reused as medical devices. **Dr. Hurley** added that Ambu is currently piloting a study with a supplier who recycles their bronchoscopes to determine how best to recycle the duodenoscopes.

Dr. Dominitz asked the manufacturers of reusable duodenoscopes to comment on the impact of sterilization on the function and durability of their scopes. **Dr. Segan** stated that all of Olympus' devices are validated for the mechanical use of high-level disinfection cycles as well as for EtO sterilization. The company has found material compatibility issues with EtO sterilization over time, with sealants, glues, and polymer parts, which is why Olympus is evaluating other methodologies.

Dr. Dominitz then asked whether flexibility was impacted, and **Dr. Segan** replied that it was not as the scopes were removed as soon as any damage was detected, which was generally limited to the sealants and glues.

Dr. Dominitz asked the number of sterilization cycles at which they were finding damage, and **Dr. Segan** was unable to comment on a specific number but said it was significantly higher than 10.

Mr. Nelson replied that FUJIFILM also provides high-level disinfection and 100% EtO gas sterilization instructions, and he commented that any type of sterilization process is

harsher than high-level disinfection and would therefore cause material degradation over repeated use.

Dr. Gualtieri inquired whether any of the manufacturers were considering a hybrid device that fell somewhere between disposable endcaps and single-use devices. **Dr. Hurley** replied that Ambu was committed to a fully disposable endoscope, while **Dr. Garrett** said that PENTAX has a number of projects in development in that area. **Mr. Vader** stated that FUJIFILM was considering all options. **Dr. Segan** stated that Olympus was considering all options as well.

Ms. Wells asked whether companies supplying single-use devices might simply refurbish the devices and call it recycling. **Dr. Dunkin** replied that Boston Scientific would work very closely with companies to ensure their participation in a solid recycling program to prevent that from happening in any way, shape, or form.

Chairman Lewis asked whether anyone had considered ultrasonic cleaning and whether it would be useful for removing contamination from any parts of the scopes. **Dr. Garrett** said that PENTAX's goal was to automate all parts of the process, however that was accomplished.

Dr. Wilcox gave an example of how jet engine manufacturers actually retain ownership of their engines and lease them to airlines while retaining responsibility for maintenance and reliability, and he wondered whether anyone had considered that as a business model. **Dr. Garrett** responded that PENTAX had instituted a program called Service Works that was a form of shared risk model. Also, the company's engagement of physicians in the maintenance cycle, he stated, has led to a marked decrease in preventable repairs. **Dr. Segan** added that Olympus has implemented programmed service and maintenance as well as a more efficient upgrade process.

Dr. Kim praised the manufacturers offering training and hands-on demonstration programs, but he felt they really needed to specify time requirements for accomplishing the reprocessing tasks so that hospitals understand how much time needed to be allotted. **Dr. Garrett** lamented the frequency with which hospitals wanted him to train people on reprocessing in under an hour, and he agreed there needed to be formal guidance on training. **Dr. Segan** reported that Olympus is working to design simpler steps and streamline the process, and he offered that as part of the validation, they could potentially include some guidance on time.

Dr. Benowitz asked what manufacturers of reusable duodenoscopes were doing to help users more easily identify devices that need to go back for maintenance or had not been adequately reprocessed. **Dr. Garrett** stated that a course in preventive maintenance aimed at physicians would be helpful.

PANEL DELIBERATIONS/FDA QUESTIONS

Dr. Haugen read the Question 1: FDA presented the currently available MDR data and the current results of the postmarket surveillance studies. FDA would like the Panel to comment on the progress made towards reducing the risk of infections from reprocessed duodenoscopes since 2015 and whether the trajectory that FDA has taken, which includes incremental improvements, such as the release of newly validated reprocessing instructions and clearance of duodenoscopes with disposable components, continues to be appropriate to

address this public health issue or whether the data indicate that more substantial changes to duodenoscopes and reprocessing methods are needed.

Ms. Dunn said that she was perplexed as to why these scopes were not better designed to be reprocessed in the field in the first place. She shared her own experience with a life-threatening infection acquired during a switch-out of a biventricular ICD device, and she urged the professionals in the room to consider the issue from a patient perspective.

Dr. Dominitz commented that the FDA has taken the issue very seriously, as well as the professional community and manufacturers, but that this is not something that can be solved overnight. He added that third-party repairs are a concern. He suggested working with the Joint Commission or other bodies on certification of personnel doing reprocessing and stated that preventive maintenance programs from manufacturers were also critical. He concluded that the FDA could do a little more, especially around third-party repairs.

Charity J. Morgan, Ph.D., commented that contamination rates seemed to be higher than the 0.4% addressed in the postmarket study data outlined in the executive summary, and she cautioned that there is not yet enough data to show whether incremental improvements were working.

Dr. Li added that MDR data in general reports less than 1% of actual device failures; therefore, if the FDA's estimated infection rate of 5% is correct, there should be 350 reports annually, which is three times the actual MDR rate. Therefore, he said, MDRs are useful but should not be used as an indicator of how bad the problem is. He pointed out that as bad as it looked, not all of the contamination may be affecting patients, and there does not seem to be a reliable way to determine whether changes in reprocessing methods would actually make a difference in outcomes.

Chairman Lewis pointed out that the greatest issue, in his opinion, was the training and monitoring and perhaps certification of the personnel doing the reprocessing of these devices. Unfortunately, he added, FDA has no jurisdiction over training.

Ms. Wells agreed that that was an essential component to the problem and lamented that the VA was unable to keep the best performing employees because they were not paid enough. She stated that a greater emphasis on education and training and better guidance from manufacturers around the length of time required for reprocessing tasks would help to professionalize the job classification.

Matthew Arduino, Dr.P.H., provided an example in which after the State of Texas officially required certification of dialysis technicians, then CMS quickly made it a national requirement. He suggested that CMS, possibly with the assistance of the Joint Commission, should be tasked with accreditation of reprocessing technicians.

Mr. Collins said he completely agreed that CMS along with accreditation agencies could set and enforce training, certification, and oversight of reprocessing staff members.

Ms. Wells said that she was glad to hear that the manufacturers were getting involved in training, but she stated that retention of reprocessing staff is also a problem due to low pay and a poor work environment. She wondered if the FDA and the manufacturers could provide guidance to healthcare facilities around setting up their reprocessing areas.

Dr. Wilcox stated that while he supported all of these ideas, his first choice was to remove the human interface altogether by either using disposable devices or, as a second choice, having manufacturers take responsibility for reprocessing. He added that another

current issue was lack of feedback in that the people doing the reprocessing were not seeing the contamination slides that had been presented earlier.

Dr. Saubolle shared that he often found that the trainers themselves were not well trained, and they were simply performing mechanical steps without understanding the reasons for each step and the consequences of skipping it.

Ashley Faulx, M.D., agreed with Dr. Li's comments about the relatively low number of infections resulting from contaminated scopes. The majority of these scopes were processed well enough that they were not making people sick. He pointed out that in the Cleveland area there are very few multidrug-resistant organisms, and he suggested that healthcare facilities in areas of outbreaks or cities with high levels of drug-resistant organisms might be more willing to migrate to newer, more expensive technologies. However, mandating these changes nationally would be a bad idea and would reduce access to ERCP. And currently, he said, the risks of these procedures were very, very low compared to the benefits.

Mr. Socola stated that currently, only four states require certification, something they were able to accomplish in New York over 4 years of working with the state health department and legislature. Therefore, it is not too difficult or expensive. IAHCSMM, he pointed out, has an excellent training and certification program that is affordable and available. Also, with regard to IFUs, he recommended FDA work with manufacturers to simplify processes and reduce the number of steps as he felt that many manufacturers were retaining outdated IFUs to simplify the 510(k) processes.

Chairman Lewis summarized the Panel's response to Question 1:

- The relative incidence of contamination leading to infection would seem to be between 1 in 300 to 1 in 700; therefore, the clinical problem is not nearly as large as the contamination would indicate, although MDRs are often underreported;
- Human factors and cleaning are dominant factors that, while not in FDA's domain, need to be addressed in terms of better training, oversight, and environmental conditions. FDA should work with the Joint Commission and other agencies to try and effect improvements in those areas;
- Improvements to duodenoscope design are already actively being worked on by the device manufacturers, and it would be difficult for the FDA to accelerate the process beyond what is already being accomplished.

Ms. Wells also wanted to recommend that manual cleaning not be phased out in favor of solely relying on AERs.

Dr. Haugen read Question 2: The Panel is asked to comment on FDA's proposal to standardize duodenoscope durability testing as a premarket bench test. FDA's proposal is to include 250 cycles of simulated use, cleaning, high-level disinfection, and terminal sterilization, to simulate use in a single year.

Chairman Lewis stated that while 250 cycles seemed to be a random number that might be too high, he felt it was a very appropriate recommendation. Multiple examples had been presented of problems with scopes, ranging from defects to wear and damage, that were

generally inadequately recognized at the clinical level.

Mr. Socola suggested building in some type of safety factor for cleaning similar to that used for sterilization, and he encouraged industry and the FDA to work together on this when validating a cleaning process.

Dr. Dominitz asked whether 250 cycles applied to both high-level disinfection and sterilization, and he pointed out that scopes undergoing sterilization might not last 250 cycles. He suggested using separate standards for the different processes.

Dr. Haugen pointed out that during her presentation she had suggested that manufacturers might want to identify a different number of cycles to be used in durability testing for scopes undergoing sterilization.

Dr. Li inquired as to what was being evaluated at the end of this number of cycles.

Dr. Haugen replied that a durability test would include a leak test, visual and other types of inspections, mechanical angulation of the device, angulation of the elevator, and an optical performance check.

Dr. Li asked whether there was any data on known failure points for these devices and, if so, how it corresponds to 250 cycles of simulated use.

Dr. Haugen explained that 250 cycles was used to estimate an annual use for duodenoscopes, which have less frequent usage than other types of GI devices, and that this proposed durability testing is seeking to develop precisely that type of data, which is otherwise currently unavailable.

Dr. Li pointed out that if the number 250 turned out to be too low, then the scope might pass durability testing at 250 cycles and then fail somewhere beyond that.

Chairman Lewis clarified that there needs to be ongoing data collection to see if the proposed 250 cycles is a number borne out by actual experience.

Dr. Burr said that durability testing missed the point. An aircraft engine, he said, is not run until failure but rather torn down and rebuilt periodically to ensure functionality. Endoscopes should be required to be periodically recertified by the manufacturer at some sort of interval where they could undergo a level of inspection that is well beyond a healthcare facility's capabilities.

Mr. Socola clarified that the FDA is simply looking for a starting point to direct durability testing, and the actual number was up to the device manufacturer. He explained the processes his labs use for durability testing, and he emphasized that the device would be inspected at multiple intervals for wear and degradation.

Dr. Dominitz added that if durability testing showed that the devices lasted through 250 cycles, it captured 90% of annual use, and therefore, an annual preventive maintenance program should be sufficient to catch any problems. Therefore, it is actually similar to a jet engine maintenance program.

Chairman Lewis summarized the Panel's response to Question 2:

- Rather than suggesting specific numbers, FDA needs to work with manufacturers to determine actual failure rates for various components;
- Since terminal sterilization is not currently being done, the appropriate standard would be for high-level disinfection.

Dr. Haugen read Question 3(a): For new technologies intended to reduce the risk of

infection from reprocessed duodenoscopes, the Panel is asked to comment on the potential for new designs to reduce the observed contamination rate, and considering that potential, the urgency with which the transition to new duodenoscope models should be made.

Chairman Lewis said he felt it was difficult to comment on his question since the removable endcaps were the only real design modification so far, and there is no data indicating whether this change will have any effects. While in theory it would allow for better access to those areas, there are other areas that are much more problematic in terms of contamination and cleaning. The only other proposed redesign is disposable devices, and therefore, urgency of transition would be a market-driven issue largely for manufacturers.

Dr. Faulx agreed that there was insufficient data on removable caps, and she pointed out that no one had found a way to make a disposable EUS probe. Therefore, she felt that healthcare facilities should not be pushed to make these changes without knowing how beneficial they are.

Dr. Dominitz pointed out that changing an equipment lease is a slow process and that he had not seen any preclinical data on disposable caps or any other modifications.

Dr. Saubolle also agreed and felt FDA and industry were moving in the right direction. Anything that could be done to smooth out the device and remove nooks and crannies would be an improvement, and he also suggested looking at materials in terms of whether or not they were more or less conducive to biofilm formation.

Ms. Wells suggested color-coding the device ports to match the appropriate brush for cleaning that port in order to simplify the cleaning process for the end user.

Ms. Meyers suggested adding mandatory time limits for flushing in the manufacturer's instructions for use.

Dr. Benowitz pointed out that although there was not a lot of data yet on disposable endcaps, their introduction was driven by the finding that fixed endcaps were retaining biomatter. Since elevator mechanisms are another area of concern, he wondered about the possibility of single-use elevator channels or single-use elevator mechanisms. He encouraged FDA and manufacturers to continue to explore these improvements rather than solely focusing on training.

Ms. Pekar voiced a concern over the issue of inadequate drying of duodenoscopes, and she pointed out that FDA does have control over instructions for use and could require manufacturers to develop more robust drying procedures or else design the scopes to not retain so much moisture.

Chairman Lewis added to his summarization of the Panel response to Question 3(a):

- There is room for improved development of more user-friendly techniques in the cleaning process;
- In addition to human-related factors, environmental factors such as using cabinets to improve drying of the devices are worth looking into as well.

Dr. Haugen read Question 3(b): FDA cleared disposable-cap duodenoscopes and then ordered those devices to be studied postmarket. For technologies that are intended to reduce contamination rates for duodenoscopes, what is the appropriate balance between demonstrating the effectiveness of the technology prior to marketing, versus the benefit of

having the technology available for use that much sooner?

Chairman Lewis was of the opinion that given the uncertainty of much of the data around all these potential modifications, there is a need for better demonstration of effectiveness prior to implementation.

Dr. Burr concurred, pointing out that the reason for demonstrating effectiveness is that the improvement then becomes marketable.

Ms. Ferriter asked whether FDA should be collecting real-world data in a premarket IDE or whether it was acceptable to review manufacturers' bench data premarket and collect real-world evidence from healthcare facilities postmarket.

Dr. Burr replied that in his opinion, an IDE is an obvious choice in order to provide solid, dependable data.

Ms. Pekar pointed out that these are 510(k) devices with a very long history, and it would be burdensome to require human clinical data for any minor changes. The appropriate thing is to do a risk-benefit analysis and let that drive the need. It should depend on the magnitude of change and associated risks and should therefore be an individual decision.

Dr. Morgan said she believes there is a benefit to both premarket and postmarket data and that the premarket data estimates the contamination rates, in the best case scenario, where the postmarket data provides real-world contamination rates. She also pointed out that ongoing postmarket studies for current devices were begun 4 years ago, and she said it makes sense to get that data before approving any new devices.

Ms. Ferriter stated that FDA has put a structure in place to get the data more quickly postmarket, which is not MDR data collection but rather a rigorously controlled study; however, she appreciated the comments and encouraged the Panelists to participate in the ongoing post-approval studies.

Dr. Haugen read Question 4: Does high-level disinfection provide an adequate margin of safety? Considering the challenges and benefits of sterilization for routine duodenoscope reprocessing, is a transition toward sterilization warranted? And if so, how can the inherent challenges with sterilization be addressed?

Ms. Meyers stated that from the viewpoint of a hospital system with no EtO sterilizers, it would be a great challenge.

Dr. Arduino pointed out that if the device cannot be cleaned adequately, both processes will fail.

Chairman Lewis agreed that where sterilization might help somewhat, if there is foreign matter or mechanical defects in the scope leading to contamination, there would be a failure rate with both processes.

Dr. Saubolle stated that sterilization would lower the bioburden so that the number of organisms would not be as high, and he pointed out that outbreaks stopped once sterilization had been implemented.

Dr. Ferriter agreed that outbreaks had stopped at facilities that had implemented sterilization.

Dr. Saubolle said that he also would rather see a lower bioburden in scopes used on

immunocompromised patients.

Dr. Kim said in his opinion the concept of sterilization was probably developed as a way of compensating for poorly cleaned or poorly reprocessed scopes. It should not be a failsafe for not doing the right thing in the first place. In his opinion, high-level disinfection is not necessarily the problem.

Dr. Li pointed out that in addition to switching to ethylene oxide sterilization, the facilities involved in the outbreaks had also retrained their personnel in cleaning. In addition, several of the outbreak facilities did not switch to ethylene oxide but simply retrained and refocused their people. Therefore, it was not clear to him that a switch to sterilization was required in order to solve the problem.

Dr. Dominitz reiterated his opinion that requiring facilities to sterilize duodenoscopes would reduce access to a lifesaving procedure.

Dr. Saubolle asked whether cultures would still be required for facilities using high-level disinfection, and he pointed out that cultures do not catch all of the positives.

Ms. Wells stated that while she strives for the highest level of decontamination possible, she strongly believes in high-level disinfection as long as it is done correctly. She added that if the AERs were to mandate a manual cleaning phase, it would drastically reduce human error and greatly increase safety.

Chairman Lewis summarized the Panel's response to Question 4:

- High-level disinfection is the appropriate standard;
- Moving to sterilization would entail a number of issues around access and cost, and is probably not warranted at the present time, given the other problems which need to be addressed.

Dr. Benowitz commented that high-level disinfection is robust enough when done properly; however, the data seems to suggest that it is rarely done properly. He added that FDA and industry have been making incremental changes and improvements in cleaning and high-level disinfection for decades, and yet there was still a problem.

Dr. Saubolle concurred and said he would feel much safer if borescopes were used regularly to inspect for damage and residue. Short of that, he still felt uncomfortable.

ADJOURN

Ms. Ferriter thanked the Panel. She concluded that FDA greatly appreciated all of the ideas and suggestions and would work towards implementation.

Dr. Schwartz thanked the Panel and assured that the recommendations would be reviewed very carefully.

Chairman Lewis thanked the Panel, adding that the diverse input had proven quite valuable. He also thanked the guest speakers, the representatives from industry, and the other Open Public Hearing speakers who had commented. He then adjourned the meeting at 4:36 p.m.

I certify that I attended this meeting on November 7, 2019 and that these minutes accurately reflect what transpired.

_____/S/_____
Patricio Garcia, M.P.H., CDR, USPHS
Designated Federal Officer

I approve the minutes of this meeting as recorded in this summary.

_____/S/_____
Frank R. Lewis, Jr., M.D.
Chairperson

Summary Prepared by

Pamela Jacobson
Free State Reporting, Inc.
1378 Cape St. Claire Road
Annapolis, MD 21409
(410) 974-0947
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