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FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

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GENERAL HOSPITAL AND PERSONAL USE DEVICES ADVISORY COMMITTEE

MEETING

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GERMICIDAL ULTRAVIOLET (UV) LIGHT AS A MODE OF DISINFECTION

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December 10, 2025

9:00 a.m. EST

Via Web Conference

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Call to Order

00:10:08 Dr. Jarvis: Good morning. I would like to call this meeting of the FDA CDRH General Hospital and Personal Use Devices Committee Meeting to order. It is now 9:00 a.m.

00:10:29 I am Dr. William Jarvis, the Chairperson of this Panel. I am currently president of Jason and Jarvis Associates, a consulting company in healthcare, epidemiology, and infectious disease. Prior to that, I spent 23 years at the Centers for Disease Control, primarily in the area of hospital infections.

00:10:53 I note for the record that the Voting Members present constitute a quorum as required by 21 C.F.R. Part 14. I would also like to add that the Panel members participating in today's meeting have received training in FDA device law and regulations. This meeting is being recorded and will be accessible to the public including the Zoom chat.

00:11:22 For today's agenda, the Committee will discuss issues related to the emerging technology in the context of medical devices, germicidal ultraviolet (UV) light as a mode of disinfection. FDA is seeking to obtain feedback to improve the total product life cycle (TPLC) evaluation of UV disinfection devices. This includes, but is not limited to, discussions around stakeholder perspective, performance testing, study design considerations, antimicrobial stewardship, regulatory considerations, and pandemic preparedness.

Panel Introductions

00:12:09 Before we begin, I would like to ask our distinguished Committee members and FDA representatives attending virtually to introduce themselves. Committee members, please turn on your video monitors if you have not already done so and unmute your microphone before you speak. When I call your name, please state your area of expertise, your position, and affiliation. Dr. Aamir Siddiqui.

00:12:40 Dr. Siddiqui: Morning. My name is Aamir Siddiqui. I'm a Plastic Surgeon in Detroit, Michigan; Associate Professor of Surgery at Michigan State University; and a member of the American Society of Plastic Surgeons.

00:12:50 Dr. Jarvis: Great. Thank you. Dr. Charity Morgan.

00:12:54 Dr. Morgan: Good morning. I'm Charity Morgan. I'm a Professor of Biostatistics at the University of Alabama at Birmingham and I specialize in clinical trial design.

00:13:04 Dr. Jarvis: Dr. Matthew Arduino.

00:13:07 Dr. Arduino: Yes, I'm Matt Arduino. I am a Public Health Microbiologist. I am currently the Senior Advisor for Environmental Hygiene and Infection Prevention at CDC in the Division of Healthcare Quality Promotion. And that's me, and I've been here for 38 years.

00:13:28 Dr. Jarvis: Thank you. Dr. Cameron Miller.

00:13:33 Dr. Miller: Morning. I am an Opticometrologist at the National-- Excuse me, National Institute of Standards and Technology, Deputy Division Chief for the Sensor Science Division.

00:13:44 Dr. Jarvis: Great. Thank you. Nancy Sauer.

00:13:48 Ms. Sauer: Hello, I'm Nancy Sauer. I'm here as the Industry Representative. My chief area of expertise is in medical device regulatory affairs. I currently work as an independent consultant under Nancy Sauer Regulatory Consulting LLC.

00:14:05 Dr. Jarvis: Great. Thank you. Rachel Brummert.

00:14:11 Ms. Brummert: Good morning. My name is Rachel Brummert. I am the Consumer Representative today.

00:14:16 Dr. Jarvis: Thank you. Debra Dunn.

00:14:20 Ms. Dunn: Hello. I'm Debra Dunn and I am the Patient Rep on the Panel today. I am a 25-year heart failure patient and I'm a national trained spokesperson for women and heart disease.

00:14:34 Dr. Jarvis: Great. Thank you. Rear Admiral Raquel Peat.

00:14:39 RDML Peat: Good morning, everyone. Rear Admiral Raquel Peat. I'm the Director for the Office of Orthopedic Devices and also the Acting Director for the Office of Surgical and Infection Control Devices. I'm a Microbiologist and I've been with FDA since 2001. Thank you.

00:14:56 Dr. Jarvis: Great. Thank you. Christopher Dugard.

00:15:00 Mr. Dugard: Good morning. My name's Chris Dugard. I'm the Division Director for the Division of Infection Control Devices in the Office of Surgical and Infection Control Devices and I am a Biologist by background. And I've been with the Agency since 2014.

00:15:15 Dr. Jarvis: All right, thank you. Katharine Segars.

00:15:18 Dr. Segars: Good morning everyone. My name is Katharine Segars. I'm the Assistant Director of the Disinfection and Reprocessing Devices Team in the Office of Surgical and Infection Control Devices. I am a Microbiologist.

00:15:30 Dr. Jarvis: Great. Thank you. Stephen Anisko.

00:15:33 Mr. Anisko: Hello, everyone. Good morning. My name is Steve Anisko. I am a Consumer Safety Officer and Acting Assistant Director for the OHT4 Sterility Devices Team. I've been with the Agency for a little over five years, and my background is in chemical engineering. Thank you.

00:15:48 Dr. Jarvis: Thank you. Evella Washington.

00:15:51 Ms. Washington: Good morning. My name is Evella Washington. I'm the Designated Federal Officer for this meeting.

00:15:58 Dr. Jarvis: Very good. Thank you all very much. Once again, I want to remind all attendees to mute their microphones until they're called upon to speak. If you have a question, please use the “raise hand” feature and unmute your microphone once I call on you.

00:16:15 Ms. Evella Washington, the Designated Federal Officer for today's General Hospital and Personal Use Devices Panel, will now provide the Conflict of Interest Statement and some introductory remarks.

Conflict of Interest Statement

00:16:29 Ms. Washington: The FDA is convening today's meeting of the Medical Devices Advisory Committee under the Federal Advisory Committee Act of 1972. The General Hospital and Personal Use Devices Panel of the Medical Devices Advisory Committee will meet virtually to deliberate and make recommendations on issues related to an emerging technology in the context of medical devices and germicidal ultraviolet light as a mode of disinfection. The FDA is seeking to obtain feedback to improve the total product life cycle evaluation of UV disinfection devices. In addition, the Committee will meet to discuss and provide advice to the FDA on devices used in pandemic preparedness and response to satisfy, in part, a requirement under the Food and Drug Omnibus Reform Act of 2022.

00:17:23 With the exception of the Industry Representative, the members of the Committee are either special or regular government employees and are subject to federal conflict of interest laws and regulations. Accordingly, FDA has reviewed the financial interest of the committee members for compliance with federal ethics and conflict of interest laws. We have screened the members for potential financial conflicts of interest related to today's meeting agenda that include their own interests and those imputed to them, including those of their spouses, minor children, and employers.

00:18:01 Based on the agenda for today's meeting and all financial interests reported by the Committee members, and in accordance with 18 U.S.C. subsection 208(b)(3), one conflict of interest waiver has been issued to Dr. William Jarvis to address his ownership of stock options in an affected firm, the current market value of which is between 1,000 and 5,000 dollars. This waiver, which is posted on FDA's website, allows Dr. Jarvis to participate fully in the Panel deliberations.

00:18:36 Nancy Sauer of Nancy Sauer Regulatory Consulting LLC is participating in this meeting as a Non-Voting Industry Representative acting on behalf of regulated industry. Consistent with Commissioner Makary's April 17, 2025 statement, FDA is only including Industry

Representatives in Advisory Committee meetings where required by statute. FDA is required to include an Industry Representative in today's meeting under 21 U.S.C. § 360c(b)(2). Industry Representatives are not appointed as special government employees nor are they regular government employees. Industry Representatives serve as Non-Voting Members of the Committee and represent all regulated industry, not any particular association, company, product, or ingredient, and bring general industry perspective to the Committee. Under FDA regulations, although a Non-Voting Member serves in a representative capacity, the Non-Voting Member shall exercise restraint in performing such functions and may not engage in unseemly advocacy or attempt to exert undue influence over the other members of the Committee.

00:20:18 Rachel Brummert is serving as the Consumer Representative for this Committee. Consumer Representatives are appointed special government employees and are screened and cleared prior to participation in the meeting. They are Non-Voting Members of the Committee.

00:20:14 FDA asks that all other participants, including the Open Public Hearing speakers, advise the Committee of any financial relationships that they have with any affected firms, its products, and if known, its direct competitors. We would like to remind the members that if the discussions involve any products or firms not already on the agenda for which an FDA participant has a personal or imputed financial interest, the participant needs to inform the DFO and exclude themselves from the discussion, and their exclusion will be noted for the record. FDA encourages all other participants to advise the Panel of any financial relationships they may have with any firms at issue. A copy of this statement will be available for review and will be included as part of the official transcript.

00:21:07 Please be advised that all participants should turn on their cameras and mute their microphones. If you wish to speak, use the "raise hand" feature at the bottom of the zoom screen and wait to be acknowledged by the Chair. Once acknowledged, you should unmute your microphone. When you are done speaking, click the "raise hand" button to lower the

hand and mute yourself again. Likewise, use this feature to notify the Chair when you need to step away from your computer and be sure to turn your camera off. To assist the transcriber when identifying who is speaking, please be sure to identify yourself each time that you speak. For press inquiries, please contact the FDA Newsroom at www.fda.gov/news-events/fda-newsroom. Thank you very much.

Opening Remarks

00:22:09 Dr. Jarvis: Thank you, Ms. Washington. At this time, Rear Admiral Raquel Peat, Acting Director of the Office of Surgical and Infection Control Devices will provide the Opening Remarks. Rear Admiral Peat.

00:22:25 RDML Peat: Good morning, and welcome to the U.S. Food and Drug Administration Advisory Committee Panel meeting. My name is Rear Admiral Raquel Peat, Director of the Office of Orthopedic Devices, Acting Director for the Office of Surgical and Infection Control Devices, and a Rear Admiral in the United States Public Health Service. I'm here today representing FDA Center for Devices and Radiological Health or CDRH. Our Division of Infection Control Devices is responsible for the review and regulation of germicidal ultraviolet (UV) medical devices. I would like to begin by recognizing and thanking the individuals on the FDA's Infection Control Medical Devices Team and other offices of FDA who have devoted many hours in preparing for this meeting. The agenda for this meeting and the executive summary have been provided and they're also available online at FDA's website. To supplement the executive summary in FDA's presentation, we've invited external speakers to provide their insights on specific topics.

00:23:38 As we look forward to discussions, there are certain aspects of the meeting that I would like to highlight for you. Germicidal ultraviolet (UV) devices are products intended to transfer electromagnetic energy from a lamp source to generate ultraviolet radiation to a microorganism, penetrating the cell walls and destroying its ability to reproduce. These

products are considered medical devices when their intended use meets the FDA's definition of a medical device, which will be discussed more in depth during the background presentation.

00:24:15 To date, we have seen an increased use of germicidal UV in healthcare environments since the COVID-19 pandemic. The Agency has seen a number of new innovations utilizing this technology as well. During the COVID-19 pandemic, we received emergency use authorization requests for UV-based technology intended to reprocess personal protective equipment, as well as other innovations, such as whole room UV disinfection devices intended to reduce contamination in larger spaces. Because of the past importance in these products during the pandemic response and its importance in innovation application, FDA is holding this Advisory Panel to fulfill a requirement under the Food and Drug Omnibus Reform Act of 2022 related to devices used in pandemic preparedness.

00:25:14 During our meeting today, we'll be discussing the regulatory history of germicidal UV medical devices; provide an overview of medical device reprocessing; discuss germicidal UV microbicidal properties, including the current clinical practices; review the current regulatory landscape of germicidal UV medical devices; and lastly discuss the current challenges for germicidal UV.

00:25:45 We hope throughout the planned presentation that the information will provoke robust discussions on the use of this technology with regards to medical devices. By thinking about the use of germicidal UV technology now instead of during the next public health emergency, we want to increase the preparedness of our healthcare community so that manufacturers can have a clear recommendation for adequately testing devices to ensure safety and effectiveness, and healthcare workers can have confidence in the use of germicidal UV technology. I would like to thank each of you for your interest and work up to this point and we look forward to an informative discussion over the course of the day.

Introduction and Background

00:26:33 Dr. Jarvis: Thank you. Now we will hear FDA's presentations on today's meeting topic. I would like to remind public observers at this meeting that while this meeting is open for public observation, public attendees may not participate except at the specific requests of the Panel Chair. Dr. Katharine Segars will begin FDA's presentation. Dr. Segars, you may begin.

00:27:03 Dr. Segars: Good morning. My name is Katharine Segars. I am a Microbiologist and an Assistant Director with the CDRH OHT4 Disinfection and Reprocessing Devices Team. I will be providing some introductory and background information ahead of today's Panel meeting. As I begin my presentation today, I would like to thank and acknowledge some of my colleagues who contributed to this content, including Mr. Stephen Anisko, Dr. Dolly Singh, Dr. Yong Xue, Dr. Lianji Jin, many of whom will be speaking to the Panel later today.

00:27:40 Today's presentation will provide a high-level introduction to germicidal UV as a medical device. We will also go over the Federal Food, Drug, and Cosmetic Act definition of a medical device. This will be followed by some brief background information about the regulatory history of germicidal UV and recent developments in this reprocessing space. I will conclude my talk with the purpose of today's meeting.

00:28:07 Germicidal ultraviolet radiation, or GUV, refers to a range of wavelengths emitted by a light source. Ultraviolet radiation is typically divided into three bands known as UV-A, UV-B and UV-C. Each band comprises a subset of wavelengths and these wavelengths exhibit various properties. UV-C has the highest energy of the three, and is commonly associated with the microbicidal properties seen in germicidal medical devices. Generally, this means that under appropriate conditions, exposure to these wavelengths can kill or disable bacteria, viruses and some fungi.

00:28:44 My colleagues will provide a more in-depth look at microbicidal GUV in subsequent presentations later this morning. For now, I'll note that germicidal ultraviolet medical devices have an important role in infection control practices. These devices may be used for microbial

reduction or disinfection to kill potentially pathogenic microorganisms and reduce associated risk of patient infection. We have seen GUV applications employed in clinical settings and home use medical devices.

00:29:16 As we discuss the various usages for germicidal UV medical devices, it is important to keep in mind the regulatory definition of a medical device, which I'll share on the next slide. We would like to highlight that the scope of today's Panel meeting pertains to GUV as a medical device and in the context of medical device intended use. A medical device is defined in section 201 of the Federal Food, Drug, and Cosmetic Act, subsection H, number 1, as an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part or accessory which is: 1. recognized in the official National Formulary or the United States Pharmacopeia, or any supplement to them; 2. intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or 3. intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals, and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term “device” does not include software functions excluded pursuant to Section 520(o).

00:30:39 With the definition of a medical device forefront, we will now review some of the regulatory landscape and context for germicidal UV medical devices. The Agency has been engaged in regulating germicidal medical device applications for UV for many years now. Some of the early regulations for germicidal UV include 21 C.F.R. 880.6710. This regulation encompasses medical ultraviolet water purifiers intended for medical purposes that are used to destroy bacteria and water by exposure to ultraviolet radiation. Another early UV regulation is 21 C.F.R. 880.6600 for ultraviolet radiation disinfection devices intended for low-level surface disinfection of non-porous equipment by dose-controlled UV radiation. 21 C.F.R. 880.6500,

which describes a medical ultraviolet air purifier as a device intended for medical purposes that is used to destroy bacteria in the air by exposure to ultraviolet radiation. There are some UV-based air purifiers that were 510(k) cleared dating back to the 1980s. While UV-based air purifiers have a long established history of use, it is important to note that historically there were fewer applications of GUV for use in reprocessing of reusable medical devices as compared to now, which is largely the reason FDA views GUV as an emerging technology. You'll hear more about regulatory requirements as well as some of the newer regulations in a later presentation.

00:32:33 Infection control considerations became increasingly prevalent during the COVID-19 pandemic, resulting in the need for more options to kill potentially harmful microorganisms and reduce pathogen exposure. In this context, GUV began to take a more prominent role in some of the newer technologies and submissions made to CDH. During a time of reduced microbicidal availability, emergency use authorizations or EUAs became a more common approach for sponsors of microbicidal decontamination and bioburden reduction devices, including GUV. To meet a public health need for availability of processing solutions, FDA sought to exercise selected safety-focused regulatory flexibilities that did specifically impact UV air purifiers and UV-based disinfection devices, among other disinfection and sterilization devices. This policy was reflected in the guidance document noted here regarding enforcement policy for sterilizers, disinfectant devices, and air purifiers. FDA also provided a webinar concerning this enforcement policy in late 2020

00:33:47 While FDA was aware of the importance of facilitating timely access to germicides, the Agency also closely monitors health and safety risks that could arise from unsafe applications of GUV technology in healthcare and home use settings. For example, FDA issued a consumer update in 2022 warning of ultraviolet wands that give off unsafe levels of UV radiation. The COVID-19 public health emergency has been expired for some time now, and EUAs are

withdrawn. Ultimately, the enforcement policy guidance document expired in November of 2023.

00:34:25 The medical device applications for germicidal UV technology have not slowed over time. This brings us to the current regulatory landscape for GUV technologies, which continue to play a prominent role in the infection control space. CDRH has seen increasingly complex regulatory submissions and manufacturers frequently reach out to the Center for feedback on UV devices with intended uses to reprocess a range of reusable medical devices, and that are intended to achieve various endpoints for microbiological kill. We continue to develop a deeper awareness of some safety risks and some benefits that GUV can provide. Over time, CDRH has begun to converge on a series of topics or questions that we believe will provide key insights to developing transparent, consistent, and scientifically-sound regulatory approaches for GUV evaluation.

00:34:22 Now, we will move on to the purpose of today's Panel. This Panel is being held to fulfill, in part, a requirement under the Food and Drug Omnibus Reform Act of 2022 related to devices used in pandemic preparedness. As we continue to build on the groundwork that has been laid regarding GUV technology, FDA is seeking the Panel's feedback on specific questions to help us address preparedness for potential future public health emergencies, including ensuring scientifically-supported timely assessment of new and emerging technologies. The questions will also guide future considerations for evaluating germicidal ultraviolet radiation technology as a microbicide for medical device applications. Our questions to the Panel were provided along with the executive summary and will be shared again during a later presentation. With the Panel's input to these questions, FDA looks forward to incorporating valuable insights from today's discussions. Here I share some of the links for information that was used to prepare this talk. This concludes my portion of today's presentation.

Overview of Medical Device Reprocessing

00:36:36 Dr. Xue: Good morning. My name is Yong Xue. I'm a Microbiologist and a Lead Reviewer in the Disinfection and Reprocessing Devices Team in the Division of Infection Control Devices, Office of Product Evaluation and Quality at the CDRH. I will begin this section with the background information on medical devices reprocessing. Following that, my colleague, Dr. Liz Bulger, our Medical Officer treating adult and pediatric infectious diseases and internal medicine, will discuss the clinical practice aspects, including the benefit and the risk of germicidal ultraviolet devices. I also want to thank my colleague Dr. Lianji Jin, who contributed to preparing and refining these slides for this presentation.

00:37:31 In this section, we will cover the following topics. I will begin with an overview of medical device reprocessing and the Spaulding classification framework, the tool we use to decide which microbial processes are appropriate. I will then introduce the current expectations for germicidal UV reprocessing, the mechanisms by which UV achieves microbial inactivation and some of the key challenges associated with the GUV technologies. Dr. Liz Bulger will then take us through the clinical perspective covering how the GUV system is being applied in practice, as well as the clinical benefits and the risks that come with their use.

00:38:21 This slide provides an overview of medical device reprocessing as outlined in FDA guidance documents. Reprocessing medical devices in the healthcare setting, validation methods and labeling. Please note that these definitions are general to medical device reprocessing and not specific to UV technology. Reprocessing refers to validated procedures used to render a medical device, which has been previously used or contaminated, fit for a subsequent single use. These processes are designed to remove soil or contaminants by cleaning, and are followed by downstream microbicidal processes, which could either be sterilization or disinfection depending on the device and its intended use.

00:39:20 Reprocessing starts with cleaning, which is a physical removal of soil and the contaminants from a device so that it can undergo further processing and ultimately be used safely for its

intended use. The cleaning step is essential because without good cleaning, downstream disinfection or sterilization may not be effective. After cleaning comes either disinfection or sterilization. So, disinfection is a process that destroys pathogens and other microorganisms by physical or chemical means. It can be further divided into three levels. High-level disinfection is a lethal process utilizing a sterilant under less than sterilizing conditions, which kills all forms of microbial life except for a large number of bacterial spores. Intermediate-level disinfection kills viruses, mycobacteria, fungi, and vegetative bacteria, but not bacterial spores. Low-level disinfection kills vegetative forms of bacteria, some fungi, and lipid viruses. Finally, at the highest level is sterilization, which means the processed device is completely free of viable microorganisms including bacterial spores.

00:40:49 How do we decide the appropriate level of reprocessing for a medical device? The Spaulding classification is the framework we use. According to Spaulding classification, the nature of medical devices could be grouped into three main categories based on the risk of infection involved in the use of the device. Critical devices are introduced into the bloodstream or contact a normally sterile tissue or body-space during use. There is a likelihood of microbial transmission and infection risk if the device is not sterile. Therefore, critical devices should be reprocessed by sterilization between uses. Examples include a surgical instrument, catheters and implants. Semi-critical devices contact intact mucous membranes or non-intact skin. While intact mucous surfaces are relatively resistant to a small number of spores, these devices should be reprocessed to be free from all microorganisms. Reprocessing should be achieved by sterilization, or at a minimum, high-level disinfection between uses. Examples include duodenoscopes and bronchoscopes. Non-critical devices contact only intact skin and do not penetrate it. They also include devices that do not directly contact the patient but may become contaminated during patient care. For these devices, thorough cleaning followed by intermediate- or low-level disinfection is generally sufficient. Examples include blood pressure cuffs and skin electrodes.

00:42:49 Now let's turn to the regulatory and validation requirements of reprocessing. As outlined in 21 C.F.R. 820.30, manufacturers of Class II and Class III medical devices, as well as certain Class I devices are required to establish and maintain design control procedures. Therefore, reprocessing instructions are expected to meet validation requirements. Each step of reprocessing: cleaning, disinfection, or sterilization needs to be validated. The cleaning step should be validated separately from the disinfection or sterilization step. When FDA reviews submissions, the scope can differ depending on the device. For some reusable medical devices, we review only the reprocessing steps provided in the instructions for use, while for other medical devices, we also expect supporting validation testing data. In general, expectations for submission of complete validation data are risk-based depending on the likelihood of microbiological contamination, of the intended use, and the reuse conditions of the reprocessed medical devices.

00:44:16 Now, let's look at how germicidal UV achieves its microbicidal effects. UV-C radiation in the 250 to 270 nanometer range is strongly germicidal. It damages microbial genetic materials, DNA and RNA forming pyrimidine dimers. These abnormal inter-site bonds disrupt the nucleic acid structure, block replication and transcription, and ultimately prevent microorganisms from reproducing. However, the germicidal effectiveness of UV varies by organism, many vegetative bacteria and viruses are inactivated at relatively low doses, while bacterial or fungal spores are much more UV resistant and they require higher or longer UV exposure to achieve kill. Finally, UV disinfection is dose dependent. A sufficient fluence of UV dose should be delivered to achieve reliable microbial inactivation.

00:45:30 While germicidal UV offers significant advantages, there are some important technological limitations that should be considered in medical device reprocessing. First, the major challenge is the line-of-sight requirement. UV radiation can only treat the surfaces that are directly illuminated, which means a shadowed area, curves or a surface blocked by other objects won't be treated. Second, UV also faces significant penetration limitations. Unlike liquid chemical

disinfectants that can saturate and penetrate throughout a device, UV cannot penetrate the lumens, porous material, or organic matter. When dirt, biological residue or a patient's soil is present, these materials can shield microorganisms from UV exposure. So, thorough cleaning is an essential prerequisite step before UV treatment. Third, the UV effectiveness varies with the distance from the UV source, surface angles, and the lamp placement. This can result in uneven microbial reduction across different areas of the same device. Finally, microorganisms pose natural defense mechanisms that enable them to repair DNA damage caused by UV exposure. Processes such as photoreactivation and excision repair mechanisms can allow microbes to recover from sub-lethal UV doses. Additionally, the extensive and repeated use of UV could potentially create selective pressure favoring organisms with enhanced UV-tolerant traits. This is why appropriate antimicrobial stewardship is important. We should use effective, validated doses, and integrate UV with cleaning and other controls to avoid selecting UV-tolerant microbial populations in the healthcare setting.

00:47:41 Dr. Bulger: Good morning. I'm Liz Bulger, an Infectious Disease Medical Officer who will be speaking to you regarding the use of germicidal UV radiation in clinical practice and hospital reprocessing. The use of GUV medical devices in clinical healthcare settings is a relatively recent and rapidly expanding area for medical reprocessing. Clinical use applications in air purification, adjunctive microbial reduction with automated robotic devices, and the disinfection of smaller reusable medical devices are a few ways that GUV technology has been used in clinical settings. For additional regulatory context, it is important to remember the FDA does not regulate the practice of medicine.

00:48:27 As with all technologies, there are use-associated benefits and risks. Let's take a moment to look at the benefit GUV provides using non-ionizing radiation to achieve microbial reduction or disinfection based on the time and intensity of exposure. Standard chemical disinfection tends to be labor- and time-intensive and can sometimes create problems for users through hazardous residues. There is an ever increasing number of new devices on the market. The

FDA is aware of possible increases in human error rates related to increasing device complexity and often heavier burden of manufacturer's instructions for cleaning and disinfection. GUV radiation, especially when delivered through an automated device, can create more simplicity, separation, and uniformity in the disinfection process. These features can make GUV a more reliable and safer technology for clinical usage.

00:49:32 Let's now move on to the clinical risks. Germicidal UV generates UV radiation whether it is being used for microbial reduction or in a disinfection process. The FDA has identified several safety concerns and every effort is made to mitigate these risks for both the user and the patient. Cumulative UV radiation exposure can have long-term impact on device materials. Over time, there can be degradation in device components, especially for plastics, rubber and fabrics. It's important to evaluate these material incompatibilities through testing to maintain the integrity of the device and ensure that it remains safe for patient use.

00:50:14 Next, there are the direct risks of UV exposure for users and patients. In this category, we'll consider two general risks, one from direct exposure to UV radiation and the other from the byproducts of UV exposure, namely reactive oxygen species like ozone. The direct effects of UV exposure on human skin, eyes and lungs can create short- and long-term clinical risks, including burns, respiratory insults, cataracts, macular degeneration, and cancers. UV light exposure can also cause increased problems for certain skin conditions, genetic predispositions, and with the use of some concomitant medications which can cause photosensitizing reactions for the patient. Reactive oxygen species like ozone need to be evaluated for their potential to cause irritation and toxicity, particularly in the lungs of chronic users.

00:51:16 It is important that microbiological and infection-related uses of GUV devices are appropriately substantiated and the device labeling is truthful and accurate. FDA is aware of the promotion of GUV devices that include unsubstantiated claims regarding the effectiveness of UV devices against specific diseases or an undemonstrated clinical benefit. The

effectiveness of GUV devices against a host of microbes including bacteria, viruses, and fungi without well-supported clinical benefit could lead to adverse outcomes for infection control in the healthcare setting. As already mentioned, the microbicidal hierarchy for UV radiation is different than for chemical disinfection. Bacterial endospores are typically the most resistant organisms for chemical disinfection, while for GUV, pigmented fungal spores tend to be the most resistant. The presence of residual fungal spores on semi-critical medical devices following UV disinfection can create increased contamination and infection risks for patients based on many device use factors. Higher risk anatomic locations, like the respiratory tract, and more vulnerable patient populations, like diabetics or immunocompromised patients, would represent areas where this change in microbicidal activity against fungus could create increased clinical concerns for infection.

00:52:52 Finally, GUV technology performs differently in the microbial reduction or disinfection space than does chemical disinfection where time and complete saturation of device surfaces is important. GUV technology works in a linear exposure fashion, so devices with complicated surfaces that create shadowing may have variable or inadequate disinfection. Reusable medical devices with complex geometries, materials, residual contamination, and soiling can represent challenging disinfection scenarios for germicidal UV and interfere with safety and effectiveness.

Regulatory History of Germicidal UV Medical Devices

00:53:34 Mr. Anisko: Hello, everybody. Good morning. My name is Stephen Anisko and I'm a Consumer Safety Officer and Acting Assistant Director with the CDRH OHT4 Sterility Devices Team. Today I'll be presenting on the regulatory history of germicidal UV medical devices as regulated by CDRH. As I begin, I also wanted to thank my colleagues within the OHT4 Sterility Devices Team who supported this presentation through preparation of content as well as providing valuable review insights.

00:54:05 Let's start with an overview of the discussion points for today's presentation. In this current presentation, I will discuss the following items related to CDRH regulation of germicidal UV medical devices. First, the regulatory framework currently in place for GUV devices will be introduced. Then, we will present the existing FDA classifications for GUV devices, including applicable regulations and device identifications. Finally, the establishment of special controls and risk management considerations will be reviewed.

00:54:42 First, I wanted to lead off with a discussion of the current regulatory framework for these products. Products that are both radiation-emitting and medical devices face unique regulatory challenges requiring compliance within two distinct regulatory frameworks. The radiation safety regulations under 21 C.F.R. 1000 through 1050 address electronic product radiation control, also known as EPRC requirements. These are intended to protect the public from hazardous radiation exposure. Additionally, standard medical device regulations ensure devices meet safety and effectiveness standards for their intended medical use. This approach was established deliberately to provide comprehensive oversight while still providing innovation and market access for compliant products. It is important to note that manufacturers must navigate both regulatory pathways simultaneously requiring both careful planning and coordination in product development.

00:55:48 Now, let's turn to some established regulatory classifications for germicidal UV medical devices. The FDA has developed specific regulatory pathways for different types of GUV medical devices based on their intended use and risk profile. The Class II designation reflects that these devices have moderate risk that can be mitigated through special controls beyond general controls. This regulatory structure provides manufacturers with clear pathways while ensuring appropriate safety and effectiveness standards. From this slide, you can see that there are currently a number of available classifications available for GUV technology products.

00:56:29 Before we get into the specifics of each of these regulations, I wanted to focus on a few important things here. First, in terms of total cleared devices, the majority of these products

listed here fall under medical UV air purifiers, and as you can see here, clearances under the regulation date back to the 1980s with a total of approximately 35 products. There has been an increased interest in the past few years for this type of device. The second item to note here is that the GUV space is growing. The last two regulations have been established within the past two and a half years. The important point here is that as the technology advances, so does the regulatory framework.

00:57:12 Now, I want to provide a more in-depth look into each of these device types with an introduction to the device type and an overview of the special controls in place for these devices, as well as discuss risk mitigations. Each classification has tailored special controls or essential performance that addresses the special risks and performance requirements for that device type. Medical UV air purifiers under 21 C.F.R. 880.6500 are intended for medical purposes to destroy bacteria in the air through exposure to UV radiation. Essential performance includes demonstration of four log reduction of the claimed microorganisms under defined operational conditions such as fan speed, room volume, and duration. UV chamber disinfection devices under 21 C.F.R. 880.6600 are intended for low-level disinfection of non-porous equipment services by exposure to UV radiation within a chamber. Special controls have been developed for this regulation.

00:58:19 And then continuing on to our most recent classifications, whole room microbial reduction devices under 21 C.F.R. 880.6510 are intended to be used to reduce microbial load on medical devices surfaces following routine cleaning and disinfection. These are Class II devices with special controls established. UV disinfection chamber devices under 21 C.F.R. 880.6511 are chamber devices intended to disinfect patient contact medical devices using UV radiation after the device has been cleaned. These are Class II devices with special controls established.

00:59:00 Finally, on the next slide, we'll provide an overview of the special controls in place for these devices and discuss established risk mitigations. Special controls were developed based on comprehensive risk assessments that identified the primary hazards associated with the device.

Performance testing requirements are extensive and include simulated use testing under worst-case conditions, incorporating factors such as soiling, room objects, distances and/or geometric complexity. Shadowing of the UV radiation is a known limitation of the technology in its ability to achieve microbicidal effect. The requirements for establishing microbial hierarchy addresses the need to understand which organisms are most resistant to UV treatment, ensuring appropriate challenged organisms for validation. Photobiological safety testing ensures that the UV lamps themselves don't pose unacceptable risks to users when safety systems fail. Material compatibility testing is critical because repeated exposure to UV radiation can degrade certain materials, potentially affecting both the treated medical devices and the GUV device itself.

01:00:15 Finally, safety interlock requirements are established to ensure that devices cannot operate in conditions where personnel might be exposed to harmful UV radiation. These special controls create a comprehensive framework that allows for innovation while maintaining rigorous safety standards. Thank you, everybody, for your time. This concludes my presentation.

Current Challenges for Germicidal UV (GUV) Medical Devices

01:00:38 Dr. Jin: Good morning. My name is Lianji Jin. I'm a Senior Reviewer in the Division of Infection Control Devices within the Office of Surgical and Infection Control Devices at CDRH. I will be providing insights into some of FDA's challenges related to germicidal UV medical devices in today's Panel meeting. Before I begin, I would like to acknowledge the many individuals from the Center for their contributions to and review of the presented materials.

01:01:13 In this section, current challenges for germicidal UV, I will cover five key topics. These include new technology considerations, hierarchy of resistance, infection prevention intended uses, antimicrobial stewardship, and pandemic preparedness. We have identified several critical areas that require Panel input.

01:01:42 Our key challenge centers on the lack of standardized testing methods for UV-C devices. Unlike chemical disinfectants, which have well-established protocols through AOAC and ASTM standards, UV-C technology presents unique testing challenges. The current landscape reveals several critical gaps. For example, a lack of accepted standard test methods specifically designed for UV-C devices making objective efficacy assessment across different devices challenging. The existing test protocols were designed for liquid chemical disinfectants and cannot be directly applied to light-based technologies. Liquid immersion methods are not applicable when dealing with UV exposure requirements. Additionally, device designs may present physical constraints. UV-C technology struggles with shadowing and penetration issues, particularly in worst-case locations like cracks, crevices and joints on medical devices. This limitation is an important consideration when evaluating the effectiveness of hard-to-reach areas.

01:03:05 Currently, we are heavily reliant on manufacturer-designed studies which vary significantly in rigor and clinical relevance. Without uniform acceptance criteria, it is challenging for the agencies to understand the performance of devices from different device makers and consistently evaluate device safety and effectiveness. Meanwhile, manufacturers do not have standard methods to streamline a process and ensure consistent and reliable assessment of microbicidal performance that meets Agency's expectations. Standardization would lower the burden collectively and would create the ability to better understand and compare the performance of devices across the landscape. Our points for discussion include developing standardized test methods specifically for germicidal UV-C devices; establishing uniform acceptance criteria for medical device reprocessing claims; and creating UV-specific performance testing protocols to thoroughly evaluate germicidal UV as a reprocessing agent.

01:04:28 Moving to our second consideration, we recognize there are knowledge gaps in understanding UV-C resistance patterns compared to the well-established hierarchy for chemical disinfectants. For chemical disinfectants, we know bacterial spores represent the most resistant

organisms and lipid viruses are among the least resistant. However, with UV-C technology, this hierarchy is not fully characterized. There is a lack of scientific consensus around which organisms represent the worst-case scenario, and resistance patterns may differ significantly from chemical disinfectants. For example, we see evidence that mycobacteria behave similarly to vegetative bacteria under UV-C exposure. Whether this is a universal phenomena is not well understood. This lack of standardization creates validation uncertainty as we have no consensus on which microbe should be used for standard validation testing. We need the expert Panel's input to help the Agency develop a scientifically-justified, clinically-relevant UV resistance hierarchy that will standardize testing expectations, support consensus standards development, and guide future research to ultimately result in medical devices that are clinically relevant, safe, and effective.

01:06:08 Healthcare-associated infections or HAIs remain a significant, preventative source of patient morbidity and mortality. These infections occur through person-to-person transmission, contact with contaminated medical devices, and contact with contaminated environmental services. Manufacturers have shown interests to develop germicidal UV-C devices based on HAIs intended uses. However, FDA has not yet seen sufficient evidence regarding the impact of automated UV microbial reduction devices on HAI acquisition. Currently, germicidal UV devices or HAI reduction are not classified by FDA, and HAI reduction intended uses typically require robust clinical data.

01:07:10 The challenge lies in study design complexity. Hospitals vary significantly in size and level of care, and it will be important to consider seasonal and geographic variation in HAI rates. We also see differences in resistance patterns, antibiotic usage, periodic infection outbreaks and variations in infection control adherence and cleaning protocols. To support HAI reduction intended uses, we need clinical data demonstrating reduction of HAI incidents directly attributable to the UV device. We are seeking expert Panel input on appropriate study designs that will assist FDA in evaluating HAI reduction or prevention intended uses.

01:08:05 Antimicrobial stewardship involves coordinated intervention designed to establish appropriate use of antimicrobial agents by promoting optimal dose regimens in clinical settings. These principles extend to all antimicrobial technologies, including emerging germicidal UV devices. As an Agency priority, we are developing our current thinking while this technology evolves. We must monitor potential signs of microbial resistance development that could eventually limit GUV technology efficacy. Our key objective is to thoroughly evaluate how GUV devices integrate into established hospital cleaning and disinfection protocols while guarding against potential microbial resistance following prolonged GUV exposure. We need expert Panel input on susceptibility testing methods, UV exposure limitations, and appropriate dose regimens to ensure we maintain the long-term effectiveness of this technology.

01:09:27 The COVID-19 pandemic highlighted the critical need for additional disinfection technologies. In March 2020, we created time-limited emergency policies that allowed device modifications without the typical authorization process and enabled the introduction of new UV devices and air purifiers while maintaining specific safety and performance expectations. These real-world applications provided valuable performance data in actual healthcare settings, revealed potential benefits of UV technologies and demonstrated the importance of proper training and safety measures. For future preparedness, we want to leverage our COVID-19 experience to strengthen pandemic preparedness capabilities and create adaptable regulatory approaches for health emergencies. We need expert Panel input to standardize testing methods for UV technologies, establish clear effectiveness measurement guidelines, and address performance against clinically relevant bacteria and viruses. Our regulatory objectives include enabling quick adaptation during health emergencies, while maintaining established safety standards and balancing emergency needs with appropriate regulatory oversight.

01:11:05 In conclusion, germicidal UV technology presents both significant opportunities and regulatory challenges. We need your expertise to address several critical areas including

standardizing testing methods, establishing resistance hierarchies, validating infection prevention claims, implementing stewardship principles, and enhancing pandemic preparedness. Your input will be essential in continuing to develop the regulatory framework that ensures the safety and effectiveness of the GUV technologies. Thank you for your attention. This concludes my presentation.

Clarifying Questions from the Panel

01:12:12 Dr. Jarvis: Thank you very much. Do any of the Panel members have any brief clarifying questions to the FDA? Dr. Siddiqui.

01:12:33 Dr. Siddiqui: Hello, Dr. Aamir Siddiqui. Thank you very much for the presentation. I had a question about the unintended consequences. You mentioned ozone. It's my understanding that there may be some other byproducts maybe in a poorly ventilated area. Do we-- Is there any regulatory agency looking at indoor pollution? Or does the FDA worry about is this a significant enough problem that it needs to be addressed or looked at?

01:13:10 Dr. Jarvis: There's someone from the FDA that'd like to address that?

01:13:16 Dr. Segars: I will start and then pause to see if my colleague, Dr. Bulger, has any additional comments. This is Katharine Segars speaking, and thank you for the question. I do think that this is an area that we are continuing to explore within our framework and scope, we do look at and are trying to be mindful of potential ozone byproducts within the regulatory requirements and limitations that we do follow. As far as other agencies that may be looking at this, I'm not sure we are prepared to speak to that today. However, I think that if there are other potential safety concerns regarding byproducts, my colleague Dr. Bulger may have more information to share on that.

01:14:02 Dr. Bulger: So yeah, I think this is a great question because we love instances where old technology raises new issues, and this is one of those places. So, I won't go on too long, but to talk at a high and a low level, we all experience UV every day, but UV-A, B and C, looking at those three kinds of UV, UV-C doesn't make it to ground, okay? So, what we're seeing now is

UV-C being used for medical purposes, and I think while that offers potential enormous advantages, we always have to be aware of the risks. And these ozone byproducts, reactive oxygen species byproducts, can cause problems when they accumulate or if you use them chronically, say in an enclosed space, as you mentioned. So, where is that an issue? Well, in a big room, not as big an issue, but next to a patient's face in a NICU incubator, the accumulation of those, or the chronic exposure that a healthcare worker might face could be important. And measuring that is difficult, so often we put that back on the sponsor to propose a way that they might evaluate that risk, and we also have ways of sort of calculating that and understanding the risk-benefit in an individual setting for an individual device.

01:15:30 Dr. Jarvis: Great. Thank you. Dr. Miller.

01:15:34 Dr. Miller: Yeah, on that last note, new to panels, the NIST Engineering Laboratory and the EPA both had active research areas in that, but due to lack of funding, they've both been shut down, so that's something unfortunate with respect to the reactive species and relationships of ventilations. My question was more on Stephen's presentation with the special controls. One of the qualifications was the nonclinical performance testing with worst-case conditions, but yet we know there's no standards for that, so what does that mean in that special control situation?

01:16:18 Mr. Anisko: So, when we're working on reviewing a submission, when we're working on a specific device, we will go back and we will look at the intended use and the specific technology like the use area, and part of that is evaluation of the worst-case conditions with the microbial reduction and the room size and exposure to materials, clinically relevant materials. These are all worst-case conditions that we do look to evaluate as part of simulated use testing. Because each device could have its own specific intended use, its own cycles, the critical process parameters will be different, so as part of that evaluation, that is definitely something that we look at for each individual submission. So, thank you.

01:17:11 Dr. Jarvis: Thank you. Dr. Arduino.

01:17:16 Dr. Arduino: Yeah. The other thing that might be helpful is to understand the roles between the two Agencies, between EPA and FDA, almost like we do for disinfectants, where there are registered products at EPA and sometimes they cross with FDA's high-level disinfectants. But understanding what EPA requires, and I think that only EPA requires that these lamps be produced in a registered facility, but there is no requirement for any sort of efficacy testing of these devices. And I think they get basically a general claim that they're a pesticide device, but there are no public health claims with those devices, as far as I know.

01:18:17 The other point here is there are two standards about doing carrier testing. And I think it's ASTM 3135 for-- And it's adapting what we do for basically chemical disinfectants and producing carriers for organisms for evaluating these devices. And I think there's a British standard, I think it's BS 86 something or other-- I can't remember all the numbers. But again, it's all about carrier testing, it's how you make the carriers, but they don't specify what organisms or anything, they don't get into that detail. And I also thought a couple of years ago that IUVA was getting together with somebody to develop a standardized way that manufacturers could test these devices, but I've heard nothing come out of that since then.

01:19:21 Dr. Miller: I can speak to that. This is Cameron once again. So, the IUVA partnered with, and we'll get into this later, I assume, the Illumination Engineering Society on how to actually measure the optical radiation coming out of the devices and to standardize, like you said, the output and measure its spatial properties of how it emits to the devices. They have not partnered, which is part of my statements later on, on the-- How do we know it's working. And the timeliness and a turnaround time of validating that it's actually functioning in its given environment.

01:20:01 Dr. Jarvis: Great. Thank you. Dr. Morgan.

01:20:05 Dr. Morgan: Hi. Charity Morgan. My question is about this idea of the healthcare-associated infection claims and how that overlaps with the practice of medicine, which is outside the scope of FDA. I understand that you're seeking feedback from the Panel on this issue of how

it relates to germicidal UV, but how are these HII reduction claims handled for other devices? It might be helpful, I guess, for me to understand sort of what we would be doing in this realm. I guess because it's-- You know, hospital infection control practices seem like they would be outside of what FDA typically regulates. Why would it be different for germicidal UV?

01:20:59 Dr. Bulger: So, I think that's a great question and something we really need your input on. The problem with healthcare-associated infections is that this is a problem that has a tremendous number of variables. So this is like, and half of you will roll your eyes at this example and half of you will sort of chuckle knowingly, but this is taking your mother's recipe for vegetable soup, and you tweak it and trying to figure out what made the difference. Okay? If you change a cup of carrots, you can't taste the difference. If you put a cup of sugar in or a cup of salt in, you see a big difference. So, what we see when we look at healthcare-acquired infections are that within a system, within a hospital, the protocols tend to be the same. There's a lot of similarity, but hospital to hospital, it varies.

01:21:57 So, when I sat on infection control boards, the healthcare-acquired infections varied because of many changes. What are those levels of care? Are you talking about a tertiary care hospital? Are you talking about a teaching hospital? Not to cast aspersions on new graduates, but who's putting in those lines? Is it somebody who does it all the time? Somebody from radiology, or is it a new intern or a medical student that changes your rates? The kinds of infections. Do you do OB? Do you do pediatric work? Even the season can change what your hospital-acquired infection rate is. Do you see a lot of people from nursing homes? What are your protocols like? What is your training? What is your oversight? And I could go on and on and on. We actually had a sort of one-time disruptor with COVID where we had fewer surgeries, fewer people coming into the hospital electively, sicker patients, more PPE. That had a big effect on healthcare, hospital-acquired infections. How do you tease that out? You can't easily, okay? That's a massive study across many hospitals, and yet somebody who's coming out with a

device wants to prove that their device makes a difference. They want to prove that their soup and their recipe is better than everybody else's. Can they make that claim? Well, it's difficult.

01:23:33 And so what we'd like from you is probably two things. What variables do you think are most important? And do you think this better lends itself to a prospective study, that is a clinical study, a clinical trial? And again, that would probably take years because there's a seasonal variation in HAIs. Or a retrospective, we put this device in, and then we did a big analysis. I think some of those things would help us figure it out. We're trying to be responsive to sponsors. They sort of want to know with any of their devices if they can affect the things that are important clinically, and HAIs are incredibly important. So, I'll stop now and let me know if that answered your question.

01:24:23 Dr. Morgan: Just a quick follow up. Has the FDA approved claims for HAI reductions for other devices in the past?

01:24:36 Dr. Bulger: We have not done that yet, except an incredibly-- Technically, the answer to that question is no, because it's such a high hurdle, novel question, new question. And remember too that the tracking for this has only become easier to do. It's different for hospitals, different for nursing facilities. The organizations that do this have now sort of coalesced and we have some guidance that's a little better as far as tracking these infections, what's important. But again, there are varieties of infections, CLABSIs, CAUTIs, ventilator infections. So, what are you making a difference with? And the landscape of microbes changes. What used to be paralyzed by MRSA now it's sort of not as big a player anymore. That landscape of resistance keeps changing. So, the impact of HAIs changes, you have to be very flexible.

01:25:40 Dr. Jarvis: Great. Thank you. Ms. Sauer.

01:25:44 Ms. Sauer: Yes, thank you, Dr. Jarvis. This is Nancy Sauer. A couple of follow-up questions related to the technical challenges that were called out in an earlier presentation related to UV-C disinfection. And I saw listed the organic residue limits the ability of UV-C to work appropriately, and that's very reasonable and appropriate, but that to my understanding, is true

of all other chemical sterilization or disinfection methods, which is why the hierarchy of always validating cleaning first. So, is there something unique to UV-C in how the organic material interacts with it? The standard cleaning validation could not cover that topic.

01:26:37 And then secondly, the ability of the ray to access surfaces and geometries and all of that. To what extent has FDA been leveraging principles of essentially dose mapping as is done in a radiation sterilization or an e-beam sterilization? Seems that there are some similarities there. Penetration is very different, but in terms of dose mapping to help characterize other lessons from radiation sterilization that we can use.

01:27:16 Dr. Segars: Thank you for your question. I'd like to start with the first item in regards to the cleaning validation and then pass to another colleague for your second question. But I think you keyed on a really critical point there. And it is expected and essential in terms of general infection control practices that thorough cleaning is needed prior to any microbial process. So in that sense, we don't consider that a unique challenge to UV. I do think projecting out as far as worst-case considerations in the event that some organic residue may have been missed, and our hope would be that validated cleaning procedures would address that. But in the worst-case event that maybe they were missed, UV being a non-contact modality may not have that kind of secondary opportunity to pick up some of those residual soils and remove them. But of course, the caveat being, as you rightly mentioned, our hope and intent would be that the thorough cleaning for any modality would remove those soils prior to the microbial process. So, hopefully that helps clarify that component. And then if I could pass to my colleague Stephen Anisko to talk about those mapping aspects.

01:28:35 Mr. Anisko: Thank you, Katie. And thanks, Nancy. This is Stephen Anisko. Just to address-- For the cleaning first, I just kind of echo what Katie was saying. It's that residue, right? And with UV, it's non ionizing, it's going to be a blocking effect. So, similar to any process, this would be an adjunct to the cleaning. In terms of a dose mapping study or some way to measure the delivered dose throughout the space, that is definitely something we would look at as part

of a review if a sponsor developed a method for that. Some of the challenges, as opposed to a sterilization step where you have a defined load and you have to find in configuration and your distribution will be known run to run to run; with these whole room microbial reduction systems, you get a varied area of the room. So, whether a patient room or an OR or another healthcare space that could vary in terms of volume, in terms of objects in the room, in terms of what's blocking that radiation. And does the bed move? Has an object been placed, is the material compatible?

01:29:51 So, all those questions. And that kind of goes back to the question earlier. And we really need to understand the specific intended use, and the specific claims, and the final finished device, and how that cycle is going to be managed, how that cycle is programmed, and what are the critical parameters and developing-- And I think that's one of the tricky parts, it's developing that validation so that a dose mapping could make sense. And definitely it could be set up into a simulated use test, but we would look to the sponsor to kind of develop that method right now. But thank you. Thank you, Nancy.

01:30:32 Dr. Jarvis: Dr. Miller.

01:30:37 Dr. Miller: Yep, I found the button. Just to clarify one question. We are talking about just surfaces. We have not mentioned anything about air disinfection, or is that part of the whole room disinfection product line? That was my question.

01:31:04 Dr. Jarvis: Someone from FDA wants to address that? If not, I guess we'll table that question.

01:31:16 RDML Peat: One moment please. We're just deliberating internally. Thank you.

01:31:20 Dr. Jarvis: Oh, okay.

01:31:22 Mr. Anisko: I apologize. I went off mute. My bad. I had a break in the signal there, Cameron. Do you mind repeating the question again?

01:31:28 Dr. Miller: Yeah, so I have two questions. One was I just wanted to clarify the scope of this Panel and discussion, we're talking about surfaces or are we talking about air and surface when we're talking about the whole room purification system?

01:31:43 Mr. Anisko: Yeah, no, good question. Good question because there is-- I understand. Yeah, there is definitely a variety of devices included in the scope of this that utilize germicidal UV. So, we have those four regulations currently in place. And if you remember, one was a chamber device for reprocessing of medical devices, and that would be surfaces. In terms of the whole room microbial reduction systems, those are an open room, but not for microbial reduction of the air, that would be specifically two surfaces, hard surfaces specifically. But there's also the regulation that's been around for a couple decades now that the air purifiers that also use UV technology, that would be used for the air. And oftentimes that's in conjunction with like a HEPA filter, but the UV is definitely a part of the technology in that case as well. So, definitely in scope, definitely in scope, air and surface depending on regulation and intended use of the device.

01:32:48 Dr. Jarvis: Thank you.

01:32:49 Dr. Miller: One more question if I have the time. So, one of the things, the separation of the device and the application is the challenging part with this GUV. For example, when the discussion was brought up earlier, the reflection of the room becomes very important in the shadowing regions. I mean, you have ceiling tiles that reflect anywhere from 3%, the 45% of the GUV light. They can make significant differences on how the functional is. How do we separate these two situations, the application versus the product that's getting the approval?

01:33:32 Mr. Anisko: Well, and I'll start with this and that's a great question because within a room-- I mean, you think about what's in a room in a healthcare space, and I had a doctor's appointment yesterday and I was checking out to see all the different items that could present a challenge. And it's definitely been one of the challenges with this, developing that validation approach to adequately establish the claims, establish that the specific device is able to make those claims.

And again, and I keep going back to simulated use, it's so hard to come up with that approach because right, they're different materials, shadowing, we know and we discussed earlier in the presentations, but that's really the thing. And it's important to remember for the whole room systems, these are an adjunct to routine cleaning and disinfection, so that microbial reductions in addition to your normal practices, your routine practices. Did that help answer? It is a challenge. The only other thing I can add there is we do include, as part of the clearance for those whole room systems, a material compatibility test. So, whatever material, and representative materials of medical device surfaces, so that is something that we have included in the risk mitigation approach and as well as evaluation. So, thank you.

01:34:58 Dr. Miller: Yeah, that’s-- I mean, it does. I'm just trying to figure out in my mind when the FDA puts it on their list, what are they saying, that it has the capability to do it?

01:35:12 Mr. Anisko: That's an excellent question

01:35:14 Dr. Miller: I'm sure there'll be more discussion on this.

01:35:18 Mr. Anisko: Yes, yes. Agreed. Thank you.

01:35:20 Dr. Gutala: Dr. Miller, this is Sreekanth Gutala here. In continuation of what my colleagues said, it’s absolutely right. UV has some limitations, right? It hits whatever it is directly exposed to. It has some poor penetration capabilities on the other side of the surface. So, we have these kinds of challenges and that's one of the reasons that we seek input from the Panel members from this workshop. Yeah, I mean, definitely it is challenging. For example, it'll not penetrate packaging materials or liquids or shadows or any crevices. If you have lumens, for example, it's very difficult to disinfect into the lumens because of poor penetration issues.

01:36:13 Dr. Miller: So, I had one question on terminology. So, in this case, when you say lumens, what's that mean? I looked up the definition. It's what I think of as optical radiation coming out of a light bulb. I understand porosity, but when you said lumens, I didn't quite understand that. Just for clarification.

01:36:38 Dr. Segars: This is Katie Segars. I'm not sure if Dr. Gutala's audio may have cut out, but I'll do my best to respond quickly and he can jump back in if I miss anything. I think that in this context, he would be referring to lumen medical devices for reprocessing which have somewhat internal or long and difficult to access components.

01:37:01 Dr. Gutala: Yeah, exactly. That's true. Thank you. I think I was speaking, but my audio was cut out.

01:37:12 Dr. Jarvis: I think we're going to have to stop there, Nancy. We'll come back and have other questions later on. We'll now take a 10-minute break. Panel members, don't forget to mute your microphones and turn off your camera. Also, do not discuss the meeting topic amongst yourselves or with anyone attending virtually. And then we will resume in 10 minutes.

Stakeholder Presentations

00:03:50 Dr. Jarvis: Welcome back. We will now begin with the speaker presentations. Each speaker has been granted 15 to 20 minutes to speak. The first speaker is Dr. Juan Gonzalez who will be presenting live. Dr. Gonzalez, you may begin.

00:04:10 Dr. Gonzalez: Good morning, everybody. My name is Juan Gonzalez. I'm the Vice President of Engineering at Xenex Disinfection Services and this morning I'm joined by Dr. Sarah Simmons. Together we worked very closely with FDA over several years in order to put in place the category, which was a brand new category, for whole room microbial reduction.

00:04:38 This morning we're going to be walking you through a few things. We're going to tell you a little bit about our LightStrike+ device, which was the first device that received De Novo authorization to operate as a whole room microbial reduction device. We'll talk about its intended use and indications for use. And then a key area that we're going to focus on are some of the things that were not only lessons learned, but great feedback that we want to be able to share, and not only with the general public but especially with our panelists so that they can get some insights as to some of the things that not only were interesting learnings, but

challenges and things that we can do to continue to improve the total product lifecycle of this brand new category.

00:05:28 But then, at the end we will focus on what we believe is a future goal for this space. We'll tell you about some of the things that we've heard within the industry, some of the things that we want to do to be able to improve that, and some of the things that we're working on with the Agency to be able to get to that point.

00:05:48 So, let's start with the LightStrike+. Xenex Disinfection Services has been operating in this space for well over a decade. We pride ourselves in being the leaders in whole room microbial reduction and we introduced the LightStrike system many years ago and have successfully deployed it across many healthcare locations throughout the world. And a few years ago, we started working very closely with FDA so that we can set this category and, in essence, set the bar for what is required to be able to be authorized and operate within this new regulatory space.

00:06:29 Our LightStrike+ is a UV device that uses xenon technology to produce broad-spectrum germicidal UV light. This high intensity pulsed light deactivates spores and bacteria which contain a lot of those key pathogens that impact the healthcare environment. We offer it in a couple of models that the hospital is able to choose depending on their use case, but in essence both of them target the same thing: microbial reduction of surfaces of non-critical medical devices. We then collect the data that these robots store so that we can then later let the hospital know just how well they're using their system within their facility. The product has the necessary safety features to terminate cycles in case anybody goes into the room while a cycle is happening. And all of these went into the design and different aspects of it are able to fulfill some of those-- Not only the general controls that were in place, but the special controls that were decided on in this work that we did together with the Agency.

00:07:45 Intended use and indications for use. This is a very, very important statement. It's been covered by some of the presentations that were given by some of the FDA panelists earlier.

And there were some really interesting questions that the panelists have posed already that we hope to be able to clarify as we go through this presentation. Again, the Xenex LightStrike+ is intended for microbial reduction of the whole room, but specifically the non-critical medical device surfaces. But this is an adjunct. It happens after the initial environmental cleaning has happened, because we need to make sure that some of that dirt and other soiling is removed and then we come on top of that in order to make sure that we reduce that pathogen load to our labeled-- To our labeled claims. Our system is used in unoccupied rooms where non-critical medical devices are present and, again, an adjunct to existing manual cleaning and disinfection practices. What I'd like to do now is hand it over to Dr. Sarah Simmons, so she can talk about some of the more microbiological aspects of what our system does.

00:09:03 Dr. Simmons: Thank you, Juan. So, I'm Dr. Sarah Simmons. I'm the Senior Director of Science here at Xenex and I performed in my laboratory all of the microbiology data that was submitted as part of the De Novo for establishing this category.

00:09:17 Some feedback we wanted to give on how that testing was done is that the volume of organisms that were required to test was, we believe, above and beyond what is actually necessary to establish the efficacy of these devices. I'm excited to hear that the Agency is talking about establishing an organism hierarchy. Some of the concerns we had specifically were the inclusion of non-hospital pathogens. These are organisms that are not relevant to the intended use environment for the device and in fact cause confusion for our customers when they're evaluating the label for the device. The reason these organisms were included is the Agency stated that having a list of only known hospital pathogens might imply a claim of infection reduction associated with the device, and we would argue that is not the case. Hospitals only care about the bacteria that are going to be present in their environment and those are the organisms that should be included in the testing hierarchy. We were also asked to include *Deinococcus radiodurans* within our testing, which is extremely UV-resistant and in no way indicative of the real-world performance of the product. We do not believe that this

organism should be included in future testing hierarchies as it's simply not relevant to how these products are going to be used in any healthcare or home setting.

00:10:39 I do know the Panel is going to discuss later the possibility of standalone use of these devices for treatment of rooms. We would not support that kind of utilization. We would be concerned about the residual organisms, while deactivated, are going to stay on that surface, potentially providing a protective environment for other organisms that are placed on those surfaces. We believe that the two-step cleaning and then use of a chemical disinfectant and then the use of UV as an adjunct is the most appropriate way to use this technology. Potentially, the UV could be a replacement for some steps at the chemical disinfection process, but a cleaning step cannot be removed from the process. That will always be necessary for UV devices to be effective. Next slide, please.

00:11:32 In the labeling requirements and safety considerations for these devices, there are some other things we think the Agency might want to include in their categories. Some lamps require significant warm-up time before reaching their full UV emissions. These warm-up times need to be considered in the label claims for these devices. This is not true for all lamps that generate UV, but it is true for some of them, so it needs to be a consideration. The labeled cycle time should not just be the maximum output needed to kill the organisms, it needs to include the warm-up time associated with these lamps because that's going to be a consideration for how these products impact the workflow of hospitals. Additionally, some lamps will require a cool-down before the device can be safely repackaged for movement to another room.

00:12:23 Large spaces will require more than one treatment. There has been a lot of discussion about shadowing within rooms. That is a key consideration for the usability of these devices. The devices need to be in multiple areas so that surfaces get direct line of sight treatment. We want to make sure the FDA is making that a clear requirement for how these devices get used. There was discussion about reflectivity of certain surfaces within the hospital and how that might

interact with the efficacy of these systems. We believe that the Agency should not consider that reflectivity because it is so variable across the hospital environments and should not impact the final efficacy claims of the devices. Next slide.

00:13:10 And finally, again to the point I just made, UV is line of sight; multiple positions should be required in rooms. These mobile devices also need to be transported across the hospital. The ergonomics of that transport needs to be considered. Some systems are very bulky and can be difficult or even dangerous for staff members to transport across certain parts of the facility. We talked on the previous slide about how lamps could become hot during use and need to be cooled down. These temperatures can sometimes be sufficient to cause contact burns for someone who may touch the lamp, either during transport or accidentally while packing it up to move to another room. So, that should be considered in the design of these devices, how are they protecting those hot surfaces from users and from patients. And proper disclosure of user interactions and identifications of those hazardous scenarios associated with them. Just making sure that the labeling is very clear on all of the hazards associated with these devices.

00:14:08 And I'll hand it back over to Juan.

00:14:10 Dr. Gonzalez: Thank you very much, Sarah. So, what's our future goal? Firstly, what we want to mention is that, as an organization, we are very happy with the work that we were able to do together with FDA over several years and continue to do as we continue to support the growth of this new regulatory category. As it was already mentioned, Xenex led the efforts to establish the QXJ product category, which is whole room microbial reduction. We were excited when this happened back in September of 2023.

00:14:49 However, there have been some challenges. We have faced several headwinds as we've been trying to grow the category. One, uptake has been minimal. We, of course, have been supplying LightStrike products to healthcare facilities all around the world and our expectation was that, once we were able to say that it was authorized by FDA, that there will be incremental growth in that uptake because, again, our ultimate goal is the improvement of

public health. There are too many individuals that are suffering because of these pathogens that are left behind, especially from the previous patient that was in a particular room.

00:15:35 Now, what could have contributed to this minimal uptake? Well, for one, regulatory messaging has been confused. Forever people were indicating, "Well, EPA is the one that regulates that space as a germicide, not FDA." There was an MOU in the past as far as where FDA came in versus where EPA came in, but it didn't necessarily apply to germicidal UV, which we are speaking about today. So, what was happening was many individuals were saying, "No, I don't have to buy an FDA-authorized product in order for me to continue to do this."

00:16:14 Also, only one other company has received clearance within this regulation, and Mr. Anisko mentioned this in his presentation, where currently there are only two products within the QXJ category; ourselves, that submitted the De Novo and set the bar, and then a subsequent company that was able to get a 510(k) clearance within that category.

00:16:41 Now, what is it that we're hearing from the market that is impacting this minimal uptake? Well, you'll see here in this presentation some very sad comments that, unfortunately, we've been hearing and that we're constantly fighting against. This is what we call those headwinds. For example, we've heard "Stopping infections is not our priority." Others, "All we have to do is manual housekeeping. We don't care if there are studies that indicate that you all are 22 times better. It costs us money to do it." This third bullet was very sad when we heard it. Some saying, "We make money even when people get sick because of these pathogens that are left behind." And lastly, "I can buy UV robots without medical device authorization." Again, you may be alarmed at some of these comments, but this is exactly what we're hearing in the industry.

00:17:38 So, what is it that we need to continue to do so that we can maximize the benefit to public health? These are all things that have to actively be worked on within this space. One, working on a reimbursement code. We want to work on making sure we're the first for enhanced

cleaning beyond manual housekeeping, because right now, unless there is a direct path to how a hospital is reimbursed for this, it makes for a very difficult sell. Yes, there are facilities that take pride in making sure that that pathogen load is down and that that risk of pathogen transmission is minimized. However, we need to make sure that it is incentivized as well.

00:18:23 The other thing: it needs to become the standard of care. In order for the uptake to happen within this space, hospitals need to be required to be able to do this. There are plenty of studies that show that many of these surfaces remain pathogenic after manual cleaning practices. We need to continue to put ourselves out there to show that this is something that needs to happen after every single discharge.

00:18:52 Our third point: clear regulatory messaging. Our hope is that this Advisory Panel meeting will help to make sure that there is clear regulatory messaging, that in order for a company to sell products that reduce the microbial load or the pathogen load on non-critical medical devices, they must have the proper clearance to be able to be sold and used. And again, our hope is that this Panel and this specific meeting is going to be able to help clear up some of that confused messaging.

00:19:33 And last but not least, something that's already been touched on. An HAI reduction claim. Even though it is clearly understood that a pathogen is a microorganism that causes infection and that if you reduce or eliminate that pathogen, you reduce the risk of an infection, we know that it is clear. Those in the know clearly know what that continuum involves. It's still something that needs to be crystal clear when we're able to make a claim.

00:20:05 Yes, there are many different pieces of work or items of work or work streams that happen within a hospital that lead to a reduction in infections and we know that whole room microbial reduction is just one of those. So, being able to put together the necessary data or the necessary clinical study to be able to prove that is something that is imperative for us to continue to increase uptake and maximize the benefit to public health.

00:20:38 We hope that our presentation this morning has helped all to get a clearer understanding of some of the things that we did to be able to establish this category in close collaboration with FDA. And we also hope that some of these headwinds we spoke about opened up some additional conversation and questions, so that together we can continue to improve the benefit of public health through whole room microbial reduction. Thank you very much for your time.

00:21:07 Dr. Jarvis: Great, thank you both very much. Our next speaker will also be presenting live. Ms. Sade Rolon, you may begin.

00:21:21 Ms. Rolon: Good morning, everyone. My name is Sade Rolon. I am an Advisory Board member for the AHE, and today I will be presenting kind of from the aspect-- From an operator's perspective as an environmental services professional, today, to continue the conversation around UV-C disinfection in the healthcare environment as an operator, from that aspect.

00:21:56 So, I'm an Advisory Board member for AHE, which is a professional member group that is under the umbrella of the American Hospital Association. Safety is our priority as environmental services professionals. You heard in the previous presentation about-- From the vendor or the sponsor perspective, about creating this safety culture, right? In our healthcare environment. That is our top initiative. And so, I wanted to have this opportunity, which I'm very grateful for, to explain some of the things that we're seeing in the industry from an operator side that has caused a lot of confusion regarding the information that has been circulated and out there since this category has since been created, right? From the information that we're receiving from sponsors as well as the guidelines that are being shared from a best practice perspective that are causing, really, concerns.

00:22:55 So, just recently we had an exchange or a summit, an AHE exchange summit, where all of our professional member groups and our individuals get together. We are comprised of over 2,500 different professionals that are in environmental services that are responsible for the safekeeping and the disinfection of the healthcare environment, right? We're the frontline

defense and the face of disinfection. So, it's very important that we're constantly interacting with sponsors and different vendors that are using devices to help us achieve those tasks within our walls, right? And so, recently, when we had an exchange, we had multiple companies that were sharing their UV devices, or UV robots, that are used all across the country and all over the world, really. There was-- Very evident that there was massive market confusion around this specific regulation. Many people were not aware of this regulation, many people were not aware of the different nuances regarding this technology, static devices versus autonomous devices, the fact that there are certain rules and regulations and a rigorous process that some vendors must go through in order to get that 510(k) clearance.

00:24:25 So, the feedback that I got as an Advisory Board member is that there are a lot of misconceptions, there's a lot of confusion, mass market confusion, around this regulation. And as the previous presenter stated, since 2023, there have only been two approved vendors with a 510(k) clearance to sell this device as a whole room microbial reduction device. There's many different robots that are out on the market. This technology is advancing and evolving every single day. But the question that I would pose is how are we using these devices and what, if any, impact and risk does that have to the operators of this device that are being utilized? As well as, ultimately, are we doing any harm because of these misconceptions and this confusion? So, I'm hoping today that we can get more clarity from this Panel and experts so that we have a clear crystal message, a transparency about how these devices are to be used in these spaces.

00:25:38 At this current state, anyone in a hospital can essentially purchase a UV device today, and that information is sometimes-- There's some misconceptions about what is effective in the environment. There is no clear universal assessment or criteria of how these devices are being vetted into the facilities and utilized on a day-in-and-day-out basis from an operations perspective. Just recently I heard, specifically, a UV device that was used-- Which was used on non-critical essential equipment inside OR suites and one of the devices caught fire. It was

not UL-tested. So, we cannot just bring any type of device inside of a hospital. The duality and the confusion around what is an EPA-registered device and what's allowed versus what is an FDA-authorized device and what is allowed. There's been some confusion there.

00:26:48 So, ultimately these devices-- We've seen an uptick since the pandemic. There was a huge, huge advancement, I guess, on the part of operators to use these devices because of COVID specifically. And so, some of these vendors and consumers are not necessarily operationalizing these devices in the intended use. So, I think that's where we, as operators and professional subject matter experts, would love to collaborate and get educational content. We would like to get clarity, specifically on what is appropriate in this space and are there any devices that are misbranded that really should fall under this category and should be operating in that capacity? In the event that we do press upon FDA authorization, is there a grandfathering process or a process into which facilities must get compliant within a certain timeframe or a duration? If that is the pathway, and they decide that these devices should be authorized and regulated, these are a lot of questions that are posed within our area. And so, we would love to have information that we could take back to our professional members group or other peoples from APIC, from our supply chain arm, the people that are-- The decision makers and key opinion leaders that are bringing these devices into our facilities and using them around patients and staff every single day.

00:28:33 So, I think there really does need to be the clarity all of the presenters and the conversations that were shared previously. This is very much a hot topic in this industry and I do believe that we need to clearly spell that out if we want to promote the health and well-being of our patients and everyone in our healthcare community.

00:28:59 So, I'm hoping that we can get that collaboration and some of these questions answered. These are coming from vendors, these are coming from operators, these are coming from infection preventionists all across the country and it is a very, very relevant topic that I think we need to address. So, with that being said, that is all that I wanted to share from the operation side to

this bigger discussion and [I] hope that we can have your partnership and support in getting those responses back to this group. Thank you.

00:29:38 Dr. Jarvis: Great. Thank you, Ms. Rolon. The last speaker is Mr. Jeffry Veenhuis. You may begin now.

00:29:51 Mr. Veenhuis: Hello, my name is Jeffry Veenhuis. I'm the President and CEO of Surfacide Manufacturing Inc, based in Waukesha, Wisconsin. I'd like to thank the Medical Devices Advisory Committee and I'm honored to present at this Panel meeting. Special thanks to Christopher Dugard, the Division Director of OHT4 at FDA. I hope my presentation today can offer a manufacturer's perspective and that it is beneficial to you all.

00:30:23 As you see, a fully accessible version of the event materials is in preparation and will be posted as soon as it's ready if you have any questions. And special thanks too to Evella Washington for helping to coordinate this.

00:30:38 So, I've spent about 30 years in leadership roles with life sciences technology companies and within the medical device industry. My experience includes implantable neurosurgical, microsurgical, orthopedic and other medical devices, intraoperative monitoring, and for the past 12 plus years, I've been at Surfacide Manufacturing Inc, where we manufacture a UV system.

00:31:08 Early on, as I got involved in the industry, I was surprised by the lack of medical device regulatory oversight and the lack of medical device regulation related to UV-C disinfection technologies. A medical device is defined as any instrument, apparatus, implant, or other similar article that is intended for use in the diagnosis, cure, the mitigation, treatment or prevention of disease. We think it is clearly applicable to UV-C microbial reduction devices. We sought clarity and after a Pre-Sub back in 2017, we began to collaborate on a De Novo. I believe the need for appropriate responsible marketing of these types of technologies demand clear, transparent disclosure of properly vetted claims for safety and for effectiveness.

Following the classification order for QXJ, the whole room microbial reduction devices, we transitioned our De Novo into a 510(k) submission.

00:32:19 Helios+ is a 253.7 nanometer wavelength, high-intensity germicidal UV-C light system intended to perform microbial reduction on non-porous, non-critical medical device surfaces, free from visual soiling and after manual cleaning and disinfection practices. Helios+ is intended for use in unoccupied operating rooms, hospital rooms and other clinical settings where non-critical medical devices are present and as an adjunct to existing manual cleaning and disinfection practices. UV-C is a direct line of sight technology. Helios+ utilizes multiple emitters to simultaneously deliver a dose to a defined area and distance. The emitters rotate and they're designed with highly reflective parabolic concentrators. Helios+ can be deployed in configurations of one, two, or three emitters.

00:33:24 As you can see here, Helios+ can be deployed in those different configurations, appropriate and applicable for the room size and shape, and can be matched with the applicable system configuration to provide microbial reduction to those prioritized medical device surfaces and other surfaces.

00:33:49 UV disinfection classification has been around for over 30 years. There are currently six primary classification codes for medical ultraviolet air purifiers, medical ultraviolet water purifiers, UV radiation chamber disinfection devices, and then you can see the QXJ classification for whole room microbial reduction device, applicable to our technology.

00:34:21 The QXJ classification identifies and defines a whole room microbial reduction device as a medical device to be used to reduce microbial load on medical device surfaces following cleaning and disinfection. We clearly understand the premarket requirement in advance of promotion, labeling and distribution for medical devices once classified. However, many UV-C device manufacturers previously marketed their products as pesticide devices and the technology has been available through or under the enforcement policy in effect during the pandemic.

00:32:02 The Environmental Services, or EVS, departments within healthcare facilities have more experience with chemical disinfectants and pesticides, and far less experience with medical devices and regulations. Similarly, many of the manufacturers serving the EVS market do not have prior medical device expertise or awareness. This has led to confusion and misinformation regarding the medical device regulatory requirements for whole room microbial reduction devices and other ultraviolet disinfection technologies used in healthcare.

00:35:42 As you can see, we successfully were deemed Substantially Equivalent through a successful 510(k) and premarket notification several months ago. As of this time, as shown here in the TPLC, there is a predicate and solely Helios+ is the only cleared Substantially Equivalent device. Many of the whole room microbial reduction devices on the market continue to actively promote and state that they're either in process or awaiting clearance, while others completely disavow their need to do so to properly promote their technology, even within healthcare spaces. The intended use of a device determines which devices fall within regulatory classification orders, but many manufacturers continue to ignore, directly undermine that this is the case.

00:36:39 The Spaulding classification and hierarchy describes a risk-based approach for requirements of applicable levels of disinfection or sterilization according to the inherent risk from the surface types or use conditions. As you can see, non-critical devices and surfaces contact intact skin and may require either intermediate or low-level disinfection. It's important to note that within the QXJ classification definition, microbial reduction devices reduced microbial loads after cleaning and disinfection of non-critical medical device surfaces. Yet the literature does show that, often, many surfaces are inadequately cleaned and disinfected during manual cleaning, and so there is tremendous value in additional microbial load reduction.

00:37:33 The classification order properly identifies the primary hazards and risks associated with the use of germicidal UV-C, all of which can be adequately and safely mitigated. Manufacturers who continue to promote and label their products without premarket review and clearance do

so at their customers' detriment. Having an established set of review criteria under special controls is appropriate and required, and we feel FDA has captured those required premarket review for all microbial reduction device manufacturers.

00:38:13 The performance testing to establish a dose hierarchy, worst-case or most-resistant organism under test in order to show and demonstrate that the device's intended use achieves the claims, was extensive, but it's also very appropriate and a basic requirement. The simulated use testing under worst-case conditions as well as the in-use or real-world performance testing are also appropriate. We learned through pre-submission, Q-subs and other AI interactions with FDA to help us to identify and achieve these testing requirements. Testing is at a significant cost and requires significant time and effort. However, we believe they're fundamental to evaluating effectiveness and safety of this type of device.

00:39:06 The photobiological safety, EMC and electrical safety biocompatibility and operating safety with proper labeling should be demanded. The long-term material compatibility of UV-C has been studied [and] can be characterized; however, there are very few current standards to test relevant devices or device surfaces. It does, however, make sense to evaluate this through required performance testing.

00:39:36 I wanted to provide a little deeper analysis on some of the key factors related to germicidal UV-C, specifically for medical device surfaces in a healthcare environment. First and foremost is that UV-C is a straight-line energy and a direct line of sight technology. The germicidal effects are greatly limited or reduced in shadowed or indirect regions. Direct delivery of energy is through a radiance when factored over time, which results in a dose. Many manufacturers focus their promotion and marketing claims solely on cycle times. However, it's really the required dose which achieves the microbial reduction and that is achieved in a validated time. And that distance is a critical factor in determining the area and/or distance to which that required dose is delivered to over time. Dose delivery to farther away surfaces takes more time.

00:40:47 Disclosing cycle time, distance, area and the validated dose is really what's required to fully evaluate UV-C microbial reduction performance. Dose values have been frequently cited in the literature and in promotion, but there are wide variations that can impact a dose requirement for microbial reduction. Different microorganisms have different resistances, and even different strains within species can vary widely in their inactivation rates by UV-C.

00:41:24 Carrier substrate, soiling, concentration and other factors can also vary the reported inactivation dose even for similar microorganisms. Labor costs are closely scrutinized in healthcare today. So, workflows or use cases that may require repositioning or require training-specific instruction is a critical parameter.

00:41:51 The final key factor is surface or device orientation. Healthcare environments have many horizontal surfaces. Most of the peer-reviewed publications and the promotion report doses or cycle times to vertically oriented surfaces and do not always include horizontal orientation.

00:42:13 I'd like to expand on that point. Helios+ and many other whole room microbial reduction devices are portable, moving from room to room with upright towers with lamps in the vertical upright plane. On the left you can see how different orientations of carriers are used in performance testing and they represent medical device surfaces, but they have different incident UV rays by their orientation. Lambert's Cosine law explains why the sun's apparent brightness changes to us on earth depending on where we are. You can see how both the height and the orientation can make a tremendous difference in UV irradiance of different orientation to surfaces. If the lamps and the surfaces are parallel or at zero degrees, the irradiance is the greatest. When the lamps and the surface are closer to perpendicular, that irradiance is diminished.

00:43:19 This depicts a similar but zoomed-in perspective illustrating how a roughened or a textured surface in combination with orientation can also impact the irradiation of a surface. In performance testing, we identified the dose required to achieve a 4-log reduction. Five different vegetative bacteria were less than 100 millijoules per centimeter squared to vertical

carriers, but it required delivery of 300 millijoules per centimeter squared to achieve that same log reduction in those same vegetative bacteria to horizontal carriers. Similarly, *C. diff* spore also required almost three times the total dose being delivered to achieve the same inactivation when going from vertical to horizontally oriented carriers.

00:44:12 Our performance testing for the 510(k) and cycle times included surfaces in the horizontal orientation. We think these are essential performances. Healthcare environments do not simply contain vertically oriented surfaces. Key microbial reduction factors, when not submitted and reviewed by FDA, have created room for misinformation and confusion within the marketplace. And manufacturers are subtly misbranding while others are much more blatant in their disregard for FDA jurisdiction and authority to regulate the whole room microbial reduction devices.

00:44:56 Here are a few examples of manufacturers perpetuating misleading or blatantly false information. One states the FDA category for whole room microbial reduction is creating confusion stating they do not focus on medical devices but environmental surfaces. They further go on to say incumbent players pursued FDA clearance mainly for marketing reasons and to create hurdles for innovative solutions to enter the market. For room disinfection robots, FDA approval does not improve patient safety, adding that their focus remains on delivering real and validated value.

00:45:43 Another claimed to be in dialogue with FDA, but yet they state: "According to FDA's response, your hospital and healthcare organization may continue to purchase and use any UV-C equipment and/or systems, including products made by our company without violating FDA regulation." While this may or may not be legally accurate, they clearly are promoting to healthcare end users, and they very much undermine and disregard the QXJ classification. And yet another manufacturer cites EPAs pesticide device regulation, potentially opening a door to promote for healthcare application of their technology.

00:46:35 Hundreds of autonomous UV-C robots have been distributed around the world and they remain aggressively promoting their products for healthcare applications today, even though none are authorized by FDA as a medical device. The robots claim they can use advanced mapping technology to create a room treatment plan and then autonomously execute that plan to deliver UV-C energy to the entire space. They exaggerate their human list or automated need for less labor and they overstate their room coverage. They understate the time required to adequately deliver a proper dose for microbial reduction to an entire space and to vertical and horizontal surfaces within a room.

00:47:30 The marketing is exaggerated puffery with deceptive misbranding. Here they claim disinfection and leaving no spot untouched, effortlessly and swiftly by completing the process two times faster than stationary devices. They claim they disinfect large spaces in less time, but yet make no transparent disclosure of a dose, delivered in a given time or of any distance or area. They claim the robot can eliminate shadowing and leave zero missed surfaces. These types of statements and claims make autonomous solutions sound too good to be true. And they are. While the technology has some advantages, like all technology, there are limits. A fair and balanced approach and a transparency of safety and effectiveness are lacking in their continued promotion to healthcare end users.

00:48:31 So, in summary, the market confusion is understandable by the past regulatory landscape and the recent proliferation of a variety of different UV-C technologies promoted during and after the pandemic. This confusion is furthered by a lack of knowledge and expertise with medical device regulations among both manufacturers and end users of UV-C microbial reduction devices. Manufacturers continue to wrongfully promote their products and they're clearly intended for use as medical devices and they're being inappropriately labeled. There's a great need for FDA premarket review of performance to ensure both safety and effectiveness. The QXJ classification demands meeting performance testing and other factors for time, distance, dose, orientation, and other critical safety parameters.

00:49:35 We appreciate that enforcement takes time and resources, and we urge FDA to continue to do so. We also appreciate that, until recently, the regulation of whole room microbial reduction devices were unchartered waters. With FDA, we learned and we exchanged information on terms like whole room and what that meant; how to define claims appropriately for the classification. We learned what performance testing is required to demonstrate and validate microbial reduction. We learned about the criticality of surface distance, of times and of orientation. We learned how to control for and accurately present performance testing across a variety of microorganisms and for a variety of use cases, configurations and conditions.

00:50:32 Our experience took us significant time and resources to successfully culminate in a cleared medical device, and we appreciate the FDA review teams' responsiveness and availability to clarify and navigate these unchartered waters. We believe all manufacturers should be required to do the same.

00:50:54 Again, I would like to thank the Medical Devices Advisory Committee for the opportunity to share our feedback and our perspectives. I believe there may be some time for Q&A, but I've also provided my contact information here for your review. Thank you.

Clarifying Questions from the Panel

00:51:13 Dr. Jarvis: Great. Thank you, Mr. Veenhuis. We have a few minutes for questions. Do the Panel members have any brief clarifying questions for any of the speakers? Dr. Siddiqui?

00:51:28 Dr. Siddiqui: Hi, Aamir Siddiqui. Two questions, I guess. One is with respect to material degradation with repeated use, I guess, what is the role from the manufacturer side informing the hospital or informing the people who make these products as to what that will be in terms of degradation? And number two is biofilm, which is the term used for bacteria that kind of live together, non-planktonic, have a polysaccharide covering over them. Do we have any data on how these devices work on biofilm? Thank you.

00:52:03 Dr. Simmons: So, this is Dr. Sarah Simmons with Xenex. Let me address material compatibility first. These devices are used intermittently within rooms, so, over a long time,

the exposure is not that great. Now, some materials are more susceptible to this damage. For example, high pressure acrylics used in hyperbaric chambers are much more sensitive to crazing damage than other materials like bed rails. The type of damage that you're most likely to see is actually discoloration of the plastics over time, fading from a white to a yellow or a brown color. There can be some cracking of those surfaces as well, depending on the type of device that is used. For biofilms, just like with the organic burden that we talked about limiting the efficacy of UV devices, if there is a biofilm present, UV devices are not going to be able to penetrate the depth of that biofilm and inactivate all the organisms that are present. They are, at best, going to get the top two or three layers of those organisms. And if the polysaccharide covering is especially thick, it will not penetrate that polysaccharide covering to get to the organisms. This is part of why we would not advocate for standalone use of UV devices. You do need that physical removal of soiling and any of those coverings in order for the UV devices to get to the organisms that are present on those surfaces.

00:53:29 Dr. Jarvis: Thank you. Mr. Veenhuis, do you have any additions?

00:53:33 Dr. Veenhuis: I agree with what Sarah said. With regard to material compatibility, there are very few standards and the body of literature is pretty scant in reports. We did do characterization through independent labs on a variety of materials that are found in healthcare spaces, both to try to, I guess, quantify the tensile strength and the diminished potential performance of those materials. There was very little performance, it was mainly cosmetic. Now, there is some other additional requirement and we labeled that very thin, single-use packages or sterile products. We recommend being removed from direct line of sight during a UV disinfection cycle just because those are susceptible by their thinness; the depth of penetration of UV is not great. And then I will add one other comment. Materials are advancing. Materials are including more UV inhibitors in them and many of them were more designed for UV-A and UV-B, but there are very beneficial to UV-C resistance as well. And I think Dr. Simmons characterized the intermittency and the cumulative dose over a lifetime

quite well. And we know that we are no more derogatory than these harmful chemicals that are being used frequently in a healthcare setting.

00:55:04 Dr. Jarvis: Great. Thank you.

Open Public Hearing

00:55:07 Dr. Jarvis: We will now proceed with the Open Public Hearing portion of the meeting. Public attendees are given an opportunity to address the Panel to present data, information or views relevant to the meeting agenda. Ms. Washington will read the Open Public Hearing Disclosure Process Statement, please.

00:55:26 Ms. Washington: Both the Food and Drug Administration and the public believe in a transparent process for information gathering and decision-making. To ensure such transparency at the Open Public Hearing session of the Advisory Committee meeting, FDA believes that it is important to understand the context of an individual's presentation. For this reason, FDA encourages you, the Open Public Hearing speaker, at the beginning of your written oral statement, to advise the Committee of any financial relationship that you may have with any company or group that may be affected by the topic of this meeting. For example, this financial information may include a company's or a group's payment for your travel, lodging, or other expenses related to your attendance at this meeting. Likewise, FDA encourages you at the beginning of your statement to advise the Committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking. Thank you.

00:56:34 Dr. Jarvis: Great. Thank you, Ms. Washington. FDA has received two requests to speak. Both speakers will be live. The first speaker is Dr. David Brenner. Dr. Brenner, you may begin now.

00:56:49 Dr. Brenner: Thank you. Okay, can you see my slides?

00:57:06 AV Support: Yeah, we see them.

00:57:07: Dr. Jarvis: Yes.

00:57:07 AV Support: They look great.

00:57:08 Dr. Brenner: Thank you. Okay, so my name is David Brenner and I'm Director of the Center for Radiological Research at Columbia University in New York, which is the oldest and largest radiological research center in this country, founded by a student of Mary Curie back in the day. Columbia University has a patent for a filter for far-UVC excimer lamps, I should disclose. So, my colleagues at UV Medical asked me to give a brief summary of far-UVC light, where it's rationale and where it stands at the moment. So, that's what I will do.

00:57:54 So, the background, as everybody at this meeting knows, is we've known for a very long time that UV-C light is very efficient at inactivating airborne pathogens. And back in the day in the 1940s, it was installed in a number of schools, and you can see actually in this left-hand picture here, a UV-C-- Commercial UV-C lamp. And it was very effective in many cases, and some results here showing it controlled a measles epidemic in Philadelphia in the early 1940s. But of course, what we now know, or we also knew then, conventional 254 nanometer germicidal UV-C is a potential health hazard to the skin and to the eyes. So, what we'd really like is a type of UV-C that can be used in occupied spaces and is still effective at inactivating airborne pathogens but doesn't have the health hazards to the skin and eyes.

00:59:04 And that's where far-UVC came to be thought about. So, conventional germicidal UV-C, as I say, is in the 250 nanometer range. If we go down in wavelength to about 220 nanometers, and that's the far-UVC range, the range or the depth of penetration of the UV-C light is much, much shorter than for conventional germicidal UV-C. So, these two cartoons here, one for skin on the left shows 222 nanometer light really can't penetrate the stratum corneum, which is the layer of dead cells right at the very surface of our skin. So, it can't reach the living cells in the epidermis, in particular the basal cells at the bottom of the epidermis.

01:00:03 And likewise the other organ that we worry about: the cornea. So, on the right is a schematic of the corneal epithelium. On the very surface of the cornea is the tear layer. And below that,

the very first layer of cells are essentially dead cells, which are going to be sloughed off into the tear layer. And again, 222 nanometer light can't penetrate the tear layer and that initial surface layer of cells, as opposed to conventional germicidal UV-C light, which certainly can.

01:00:57 So, that's the general idea behind far-UVC, that it's potentially as effective at killing pathogens, which are very small and certainly can be penetrated by far-UVC, but it's potentially-- It's going to be safer for human exposure, both to the skin and the eye.

01:01:20 So, there are only two questions: is it safe and does it work? And I'll talk a little bit about both of those.

01:01:28 So, does it work? Well, let's talk about a couple of scenarios. Does it reduce the level of pathogens in room air, in occupied room air? And what about surgical site infections and hospital-acquired infections? So, answer the question, well, is it--? Does it reduce the level of airborne pathogens in occupied rooms? Well, in those studies which have been published so far, the answer is essentially yes. This particular study was in a mouse cage cleaning room, where there is a very high level of airborne murine norovirus in the room, and it's an occupied room, people are coming in and out all the time. And after far-UVC was installed, the level of airborne murine norovirus was decreased by more than 99%. So, encouraging.

01:02:36 Surgical site infections. Well, let me talk first about the role of conventional UV-C. So, conventional 254 nanometer UV-C has been used extensively over many years in operating rooms to reduce surgical site infection. And the average over 10 major studies of the surgical site infection rate was about 80%. So, [it is] very encouraging. But the need for cumbersome protective clothing when we're using conventional germicidal UV-C really limited its use in the operating room. So, the thinking is, well, far-UVC is potentially going to be equally effective at reducing surgical site infections, but without that need for cumbersome protective clothing.

01:03:34 And far-UVC has been studied in a mouse-wound model and does indeed have the properties that we want in terms of both efficacy and in terms of safety. And it's now being installed in a number of operating rooms worldwide.

01:04:01 Yeah, and there's one-- There is also one study in King Hamad University in Bahrain with about a 50% reduction in surgical site infections after far-UVC was installed in the operating rooms. Encouraging.

01:04:20 In the more general context of hospital-acquired infections, so, far-UVC has been installed in many hospitals worldwide, and this certainly is not a complete list. It's a list of some of the ones I know about. They've been installed, really, only in the past few years. So, there really isn't much long-term data to report on at this point. We'll point out one study in Cairo where the hospital-acquired infections in their ICUs were reduced to zero.

01:04:57 So, this is the potential evidence of efficacy, but of course the real issue is: is it safe? And there are three lines of discussion there. One is the biophysics, and I've talked about that, that it simply has a shorter range, so it can't penetrate through our stratum corneum in the skin, [it] can't penetrate the tear layer in the very first layer of superficial cells in the cornea. But beyond that, as everybody here knows, there are existing national and international safety regulatory frameworks. I'll talk a little bit about that. And then about the little survey of the published safety studies that have gone on.

01:05:49 So, we all were probably familiar with a graph like this, which is the threshold level values, the TLVs, that ACGIH comes up with as a function of wavelength. And this was their pre-2023 graph. And then, in 2023, because of the plethora of far-UVC experimental data which had appeared both of the skin and the eye, they modified their TLVs. And that's the green curve and the red curve. So, basically increased the TLVs in the far-UVC range while really not changing it in the higher wavelength ranges. And following that, that 2023 change in the TLVs, there was a change in the IES/ANSI standards and correspondingly UL equipment standards.

01:06:57 So, let me talk now for a few minutes about skin and eye safety studies. And again, in no way can I be comprehensive about this because it's really a pretty large field now. And there's an annual international conference; ICFUST, international conference on far-UVC safety and technology, I think. Again, in terms of skin safety, this is one of the more direct studies, actually it comes from Columbia University, where we use monochromatic wavelengths and look for DNA damage in a human skin model. What the graph is showing here is the level of CPD damage, which is one of the UV-specific DNA damage types, in the epidermis as a function of wavelength. And again, what you see is essentially nothing in the far-UVC wavelength region. And then as you move to the conventional germicidal UV wavelength region, not surprisingly you start to see DNA damage.

01:08:13 And not surprisingly, all the factors that you might worry about, like age and sex and melanin and ethnicity and Fitzpatrick scales, really don't have any significant effect on 222 nanometer skin response. And that's simply because the way it works is that the far-UVC isn't reaching the epidermis. So, you wouldn't expect any of these factors, really, to be important. But there have been quite a lot of studies basically using skin samples from human surgeries, which actually demonstrate that that's the case. Again, by no means a complete survey of skin safety studies.

01:09:00 So, moving to eye safety studies, as I said, the protective layer in the eye is both the tear layer and the surface of the cornea and the very first layer of superficial cells, which are essentially dead cells, which are basically shedding into the tear layer. And I would just make the point here that actually the human eye is partially shielded from any type of overhead light by the brow and the forehead. And there've been numerous studies in the context of sunlight about that. And, in general, the numbers that we've come up with, which others have fairly similar numbers, that the average eye dose of someone who's walking around in a room with overhead lights, is about 6% of the maximum skin dose, shall we say, to the top of the head. So, there's automatically some level of ocular protection there.

01:10:03 But again, looking as a function of wavelength, again, using a laboratory corneal model, without a tear layer, I should say, in this case, what you see in the bottom left graph here is, again, the measure of DNA damage in the cornea, in different layers of the cornea, as a function of wavelength. In that very first superficial layer, you certainly see DNA damage. In this case we don't have a tear layer here. But again, there's not so much concern about that very top superficial layer in the cornea because they are dead cells, which are in the process of being sloughed off into the tear layer. But that one goes deeper into the wing layer and the basal cells. Again, you don't see damage in the far-UVC range, but as you get into the conventional germicidal UV range, you certainly do, in the paper published on the right here.

01:11:08 And those were done with laboratory human skin and human corneal 3D models. To an extent, you can do the same thing with human corneas. And this is a study with human corneas that were kindly donated from the New York Eye Bank. And again, looking at far-UVC damage versus conventional 254 nanometer damage, if you look at the XZ-projection here, so, basically [what] you're looking at now is a function of depth in the cornea. For 222 nanometers light you see damage absolutely in the very top layer of the cornea, the superficial layer of cells, but you don't see any damage deeper down. Whereas with conventional germicidal 254 nanometer light, you can see damage basically all the way through the cornea.

01:12:12 And there have been a number, now, of far-UVC ocular safety studies actually in rooms. And just so a couple here. One in Scotland looking at short-term ocular discomfort. And basically, they did not observe any when they had-- So, there are people in the room of course. And a longer-term study in Japan, a medical exam room. Again, they did not report any long-term adverse ocular effects.

01:12:49 So, essentially all the studies that I've talked about have looked at far-UVC exposed over a fairly short period of time. Whereas of course, what we'd need to think about is far-UVC exposed over a long period of time. So, at Columbia, we did a study where we basically exposed hairless mice to far-UVC over a period of a total of 66 weeks, so, a year and a bit,

giving a variety of different doses to the-- Far-UVC doses to the mice, and an eight-hour-per-day, five-days-a-week exposure. So, these are not genetically different mice, these are simply mice that don't have any hair. So, [it is] very useful for our studies.

01:13:45 And we looked at skin and eye effects after this very long exposure for a variety of different doses, some of which were low and some of which were actually larger than the regulatory limits. And we didn't see any evidence of induced skin cancer or any of those skin abnormalities after chronic exposure at any dose. So, there were no differences between the control animals and the exposed animals.

01:14:16 And likewise for the eye. We did studies in terms of detectable eye pathology or looking at actual visual deficits. And again, we didn't see any effects after this very long exposure. Again, not surprising because of the limited penetration of far-UVC light.

01:14:40 And the final issue I just want to talk about for a moment is the issue of changes in air quality. And yeah, I'm very, very happy to see Cam Miller on this call who's one of the real experts in this area. So, the initial studies were done in test chambers, but more recent studies have been done in real-life rooms, and that's clearly a better study to do. So, I'm going to just show a couple of actually fairly large numbers of studies that have taken place. This is one in a-- From the University of Maryland in a Baltimore hotel room with far-UVC lights installed. And they looked at the change in indoor ozone concentrations for the far-UVC lamps and found an increase of about six parts per billion. And that's about typical in general for the far-UVC lights. So, a very slight increase of less than 10 parts per billion typically, in most settings. They did not see an increase in ultrafine particles when they turned the light-- Oops. They did not see an increase in ultrafine particle concentration in the air when they turned the lights on. And in fact, actually they saw a decrease, which probably was associated with outdoor changes.

01:16:16 And a similar study in a New York City conference room, again, in typical settings and air changes per hour of 1.3, which is average, and a typical far-UVC exposure. Essentially, this

study was looking at particle counts with the far-UVC lights on and off, with a fancy particle counter, which could measure particulates in the nanometer range up to the micrometer range. And basically they really didn't see anything, averaged over all the particle sizes, which is what you see in the left-hand graph. And in the right-hand graph where it was broken down into particle sizes, again, you really didn't see anything in the nanometer range or the micrometer range.

01:17:15 And at Columbia, we've been trying to look at this rather more systematically. So, we have a room specifically designed for this study. It's meant to be a real-life room, so it's got carpets and sofas and bookshelves and the like. But we control far-UV exposure. We can control the changes per hour, we can control changes in humidity, and do as many measurements as we want. And what we're really seeing is that changes in indoor air quality are really significant only if you operate the far-UVC lamps well above the current regulatory dose limits, which absolutely one should not, and in very, very airtight rooms.

01:18:04 So, I'll just conclude that far-UVC is pretty promising as a practical option to markedly and safely reduce airborne viral loads in occupied indoor locations. And I messed up the word occupied there, but that's the key. These are designed to be used in occupied indoor locations. Extensive evidence for skin and ocular safety, again, when used within the current regulatory limits. We don't think there are going to be significant air quality issues, again, with when you use real-world rooms, with real-world ventilation rates and use with the current TLVs. And the early efficacy results, I would say are certainly pretty promising, both in the rooms outside of the hospital and within hospital settings. And there I think my time is up and I will stop there.

01:19:04 Dr. Jarvis: Thank you, Dr. Brenner. The next speaker is Mr. Gary Kellstrom. Mr. Kellstrom, you can begin now.

01:19:11 Mr. Kellstrom: Thank you very much and almost good afternoon to everybody. Good morning. Give me one second to pull up my presentation here. Not sure what happened to it. There it is, Alright. So, I'm Gary Kellstrom, the CEO and Founder of Geared Power Biotech.

We're a small early stage company working to commercialize our first product. And [I'll] advance to the next slide here.

01:19:43 In our experience, medical device innovation is alive and well. I think we're seeing a lot of that here today. The FDA is engaged and helpful in moving innovative devices forward, even if it requires more interaction and discussion about indications for use, populations at risk, meeting statutory requirements. Our product, BioGuard UVC, is an award-winning transformative technology. We have congressional support for military and consumer use through the two appropriations bills listed there. It's potentially market-dominant in healthcare settings where pathogenic risks are elevated. We are specifically looking to reduce HAIs in emergency departments. It's a possible candidate for inclusion in the Strategic National Stockpile for pandemic response.

01:20:31 So, working with the FDA, we've taken a novel approach to respiratory infection control. We inactivate the pathogens in the exhaled breath of infected individuals, or otherwise known as source control. The FDA recognizes its potentials, working with us to address potential deficiencies in our application related to statutory requirements. For example, the population defined in indications for use is the infected patient. In our case, we refer to it as the pathogen reservoir. While population at risk is not just the patient, but everyone in the room. All of the susceptible hosts, medical staff, as well as other patients. So, the Breakthrough Device statute seems to have been written to require the population at risk to be the patient. And so, those are some of the challenges that we've got. They're not insurmountable, but these are challenges.

01:21:23 And here's some additional challenges based on our novel approach. We have non-filtered protection. And I heard other speakers speak of this, I apologize for not recalling their names. But unlike other PPE, there is no standard for testing with UV-C devices. We're not measuring particles, so we can't use those standards or that kind of equipment. We have a focus on public health, preventing pathogens becoming environmental contaminants. So, we're protecting

everyone in the room rather than just the patient. The patient benefits as well, but it's a broader population.

01:22:02 We have a claim that it's going to boost natural immunity by allowing safe mucosal exposure to inactivated pathogens. Note the claim at the bottom. These haven't been cleared by the FDA yet. And then we're pathogen agnostic. Another challenge is the Breakthrough Device designation required a specific disease to be identified. So, these are just some of those challenges that we ran into.

01:22:28 However, on the wonderful side, the FDA has been tremendously responsive. We utilized the DICE hotline, they were excited about the device's potential. That was very encouraging. FDA's response has been encouraging. Same-day emails, 10-day response to our eSTAR application, interactive review status, being invited to speak on this Advisory Committee. Thank you very much. And the current status of our designation, our Breakthrough Device designation is still pending.

01:23:01 Specific comments that we wanted to share here. We're proud to be working with the FDA to obtain clearance for BioGuard UVC. We're also grateful for the special consideration afforded to startups navigating the De Novo process, including the Early Payor Feedback Program. Those insurance codes are critical to the commercial success. We believe BioGuard UVC will transform respiratory infection control. Therefore, it's of strategic importance that the FDA continues to receive program funding. We also believe considerations should be given to allow FDA the operational discretion to expand such programs to include future innovations that might not have been anticipated at the time of writing of guiding statutes. I know that's a challenging one, but it's pertinent to our discussion here today.

01:23:53 And finally, I just wanted to thank the Committee and Evelyn-- Evella. I'm sorry. Evella Washington for allowing me to have this time. Thank you.

Clarifying Questions from the Panel

01:24:06 Dr. Jarvis: Thank you, Mr. Kellstrom. I now pronounce the Open Public Hearing to be officially closed and I wonder if the Panel has any questions of the OPH speakers. Dr. Arduino?

01:24:33 Dr. Arduino: Yes, this is Matt Arduino. And this goes back to the far-UV. I've seen some proposing to use this type of technology for continuous room disinfection, for actually treating surfaces on a continuous basis by-- Depending on how the lamps are placed in a room. Is that another way that this technology could be eventually used?

01:25:09 Dr. Brenner: Yeah, thanks for the question. So, it certainly-- Far-UVC was certainly initially thought about in terms of airborne disease inactivation, but of course it does inactivate surfaces when it has the line of sight, but it doesn't inactivate surfaces where you don't have the line of sight. So, I think it's an adjunct to its primary function, which is airborne disinfection, I would say. If you are specifically trying to do a surface inactivation, you can certainly aim it specifically at that surface. But in general, I think it's more airborne in its motivation.

01:25:55 Dr. Arduino: Thank you.

01:25:55 Dr. Jarvis: Ms. Sauer.

01:26:00 Ms. Sauer: Thank you. This is Nancy Sauer. A question for Dr. Brenner. In the study with the hairless mice, you had a negative control of no exposure, and then you had a defined period of time, but there was no positive control with a longer wavelength UV. And so, it is a little hard to interpret how much of a difference in how powered that study was. Do you have any information on that expected timeframe and incidence of skin cancer in that animal model with longer wavelengths of UV-C?

01:26:36 Dr. Brenner: Well, I mean there's a history of those sorts of studies with conventional UV-C going back many years. And certainly I think if we'd done those-- We didn't do them, you're absolutely right. Had we done those studies with conventional UV-C, absolutely we would've

seen skin cancers. Yes, I think it would've been lovely to have done those positive controls. I don't think we had the-- Didn't have the funds to do that. It would be great in the future to do a head-to-head in terms of far-UVC and conventional UV-C.

01:27:21 Dr. Jarvis: Great, thank you.

01:27:22 Dr. Brenner: I should say, in shorter term studies, we've certainly compared far-UVC with conventional UV-C in those mass models and certainly seen a major difference.

01:27:39 Dr. Jarvis: Great, thank you. We will now take a one-hour lunch break. Council members, please do not discuss the meeting topic during lunch amongst yourselves or with anyone attending virtually. We will resume in one hour, which is two minutes after one.

FDA Questions to the Panel

00:08:29 Dr. Jarvis: Welcome back, everybody. It's a little bit after 1:00 p.m. and I'd like to resume this Panel meeting. At this time, let's focus our discussion on the FDA's questions. Panel members, copies of the questions are in your Panel packs. I would ask that each Panel member identify him or herself each time he or she speaks to facilitate transcription. Dr. Dolly Singh will read the FDA questions, after which we will address each one separately.

00:09:04 Dr. Singh: Morning, my name is Dolly Singh. I am a Biochemist and Microbiologist and the Team Lead of the Disinfection and Reprocessing Devices Team in the Division of Infection Control Devices in OHT4, Office of Product Evaluation and Quality in the Center for Devices and Radiological Health. I will share the questions for which the Agency is seeking Panel input.

00:09:31 Panel Question 1: "To date, the Agency has only authorized UV devices to support medical device reprocessing for general microbial reduction or high-level disinfection under specific conditions. The Agency believes device innovation may support additional indications in the future, such as standalone disinfection, which may result in different disinfection practices in healthcare settings. However, the FDA also believes that UV as a germicide for medical device reprocessing has known technological limitations (i.e., shadowing, low penetration)

which may challenge the ability for manufacturers to support standalone disinfection intended uses with appropriate safety and effectiveness data."

00:10:27 Panel Question 1a: "Does the Panel have recommendations on performance testing specific for UV radiation reprocessing of medical devices that may support a standalone disinfection intended use?"

00:10:46: Panel Question 1b: "In addition, manufacturers may also be interested in reducing or preventing Healthcare-Associated Infections, known as HAI, indications. The Agency has typically recommended a clinical study to support such indications. However, the FDA recognizes there may be challenges in designing this type of clinical study such as inconsistent infection control practices across clinical settings, variability in reprocessing techniques and appropriate control conditions. What recommendations does the Panel have regarding study design considerations to support indications such as reduction or prevention of HAIs?"

00:11:40 Panel Question 2: "To support appropriate performance testing, the Agency currently asks manufacturers to determine an appropriate hierarchy of microbial resistance to germicidal UV for reprocessing of medical devices. To avoid development of a level of evidence that may be specific to individual UV devices, FDA is seeking recommendations on a scientifically justified consensus for level of evidence that should be established for germicidal UV hierarchy that could be applied across the device type without individual manufacturers developing new hierarchy testing for each new device. Does the Panel have recommendations on what information would be needed to support a general hierarchy of resistance for UV?"

00:12:35 Panel Question 3: "With increasing use of germicidal UV devices to reprocess medical devices in clinical settings, as with any frequently used antimicrobial agent, increased antimicrobial resistance is a major public health consideration. As it relates to UV safety and effectiveness of medical devices, what susceptibility testing, exposure limitations, and/or review aspects should be considered to support antimicrobial stewardship to guard against potential emergence of UV resistance amongst clinically relevant microorganisms? Does the Panel have

suggestions of ways UV devices could be used in conjunction with existing practices that would help mitigate the rise of UV resistance?"

00:13:33 Panel Question 4: "During the COVID-19 public health emergency, certain Emergency Use Authorizations (EUAs) utilized UV as the primary microbicidal agent. Example, UV decontamination systems used to reprocess personal protective equipment, also known as PPE. In addition, the Agency has seen an increase in innovation related to UV technologies as a mode of disinfection for medical devices. Increased innovation could lead to confusion regarding how such products fit within the overall landscape of devices intended for infection control. What information is helpful to healthcare providers to promote transparency and improve comprehension for the intended users for which these technologies are currently authorized?"

00:14:34 Panel Question 5: "What other considerations for innovations in germicidal UV reprocessing of medical devices does the Panel recommend?"

00:14:46 Thank you for your time and we look forward to hearing your feedback.

Panel Deliberations

00:14:53 Dr. Jarvis: Thank you, Dr. Singh. We will now begin the Panel deliberations. Panelists, please identify yourself each time you speak to assist the transcriptionist with identifying the speakers. Also, please use the raised-hand feature. Once I acknowledge your hand, unmute your microphone and then mute it once you are done speaking. If we could have the first question up, please. And I think, Ms. Sauer, I cut you off earlier with the question, but I think before we begin these questions it might be worthwhile you stating what you were going to raise?

00:15:40 Ms. Sauer: Yes, yes, [I] will be happy to do so. And I was just about to raise my hand for a specific question here, too, but-- Right. There's all this ecosystem and variety of devices that are being discussed today and that we heard in the Open Public Comment period. So, I would just put out a request that with any comments we're making that we're very clear if this is

something that would apply to all. Are we talking about a chamber disinfection device? Are we talking about whole room? So that we can just all keep this complexity in mind. And then a clarifying question I had with regard to this Question 1, standalone disinfection. This would not preclude cleaning and then disinfection, correct? It's just that it would be the sole disinfecting step. Am I correct in my understanding of that?

00:16:37 Dr. Segars: I can jump in. Yes, that is a correct understanding. To clarify, we are not suggesting to preclude cleaning. This would be simply a standalone disinfection, but would still include a cleaning step separately.

00:16:53 Dr. Jarvis: And then, I guess, the question comes back to Ms. Sauer's on, A, where you say "performance testing specific for UV radiation reprocessing of medical devices," is that specifically like a chamber for doing probe disinfection? Or is that including that and room disinfection? Or just room disinfection?

00:17:33 Dr. Segars: This is Katie Segars. Could you please clarify the question? Was that directed to-- And who it was directed to? If it was to FDA or the Panel?

00:17:41 Dr. Jarvis: No, to the FDA. [Does] Anybody from the FDA want to address that? Because I think otherwise it's unclear. Are we talking about everything or are we talking about specifically just the disinfection--? For instance, what you have down there, for me, at least, as a clinician, medical devices, I don't think of a room as a medical device. I think of a vaginal probe being a medical device or a N95 respirator being a medical device. So, when you use that term, how are you asking this question? Is it specifically disinfection of a device that will be used in a patient? Or are we talking about the patient room as well?

00:18:36 Dr. Segars: This is Katie Segars. I'll start and then see if any of my colleagues want to add anything. But I think you all have really encapsulated one of the challenges that we're looking at with the overall topic of germicidal UV. This is kind of something that we've discussed internally quite a bit and we also really welcome the Panel's feedback on teasing that very question out. So as you mentioned, there are different types of medical devices that may need

to be reprocessed. And as we heard in some earlier presentations, the level of reprocessing of microbicidal processes will typically depend on the type of patient contact. And in particular we would often look at a modified Spaulding classification to kind of make that assessment.

00:19:18 So, with this question, one of the things that we're trying to get at here is we have seen some of these, as was described earlier, microbial reduction devices that are supplemental or adjunctive to disinfection. But we are also aware of some of these technological limitations that have been discussed in some earlier presentations as well that present challenges to such implementation as the only disinfection process. Again, not to replace cleaning, but in terms of being the only microbicidal process rather than an adjunct. And in digging deeper into that and what are the questions and performance-testing specifications that you might recommend that we consider to support moving from an adjunctive type of indication to a standalone indication, I believe Dr. Bulger may have some additional clinical perspective to share. I can pass to her.

00:20:20 Dr. Bulger: Yes, so, I think you've hit on something that is really important and part of the reason we asked you to comment and not to make you be all things to all people. If you want to clarify what you're addressing, we get that. We see devices for everything. We see devices for air, for the environment, for patients. We see skin-wound devices. And as you said Dr. Jarvis, it matters whether that's an ultrasound vaginal probe or a bronchoscope. And the limitations, the problems, the burden of proof are all difficult. And add to that, the tools we have for other kinds of disinfection don't work in the UVC space. So, it's all those things that then go into the final bucket often of healthcare-acquired infections patient impact, but it's a very old technology trying to cover a lot of real estate in new ways. And you're right, the burden of proof is different in every siloed device, every bit of performance testing.

00:21:31 Dr. Jarvis: Great. Thank you. Dr. Morgan.

0:21:36 Dr. Morgan: So, sort of to build off of Dr. Jarvis's point about getting away from thinking about the room because the room is not the medical device, but the objects in the room that are

going to be cleaned by the-- I'm thinking of the whole room devices at this point. In terms of performance standards, I think that a place to start is the studies could focus on what is going to be in a typical room that would be cleaned by one of these whole room devices. And you can compare how successful the disinfection was for one that was in a room with the device versus one that was disinfected from the traditional chemical disinfection. And that would give us a starting place for "Are these whole room devices successful?" And because what worries me most about the whole room devices is that these rooms are going to be so variable in how they're laid out, and not only the actual rooms themselves will be different from clinical setting to clinical setting, but the positions of the medical devices in the rooms will be changing as different clinical staff set the room up between patients. So, the probe might be in one spot in the room earlier in the day and it's been put somewhere else later on and now the dose has changed based on where it's been moved in the room. So, I think instead of thinking about "Do these UV devices disinfect the room?," what we really want to know is "Do they disinfect the objects in the room?" And that's what we want to compare in a clinical study.

00:23:32 Dr. Jarvis: Dr. Miller?

00:23:36 Dr. Miller: Yes, there seems to be-- I mean, one of the things-- When you look at these devices, because they're not directly in the application, the only thing the FDA can say is whether it is capable of doing it in many ways. Did it pass a standardized performance test such that the device is capable of doing it? And the discussions I've had with other folks-- What we really need is some sort of validation methodology in the application, which is not the purview of the FDA. Something where I can do a 30-minute, one-hour PCR test looking for one pathogen or something I'm really concerned about, *C. diff* or something like that, *C. difficile*, excuse me, in the application. So, trying to think of what the FDA can do is-- The final result is stating that it is capable of disinfection if applied correctly, but there's still that validation step which requires, as Dr. Morgan said, I need to know it worked as the end use,

which is not the purview of the FDA, but as a society we need that quick test, which from what I understand doesn't really exist to the level we'd like it to. [Indiscernible 00:24:57].

00:25:02 Dr. Jarvis: Ms. Sauer?

0:25:05 Ms. Sauer: Yes, just a few thoughts here from industry perspective. A lot of attention rightly to the newer and more challenging whole room robots, that may be a more challenging path to get to an ability to claim that it can cover all the disinfection as opposed to being an adjunct to chemicals. I would just like to put a couple of thoughts out there. For industry, the more that we can not reinvent the wheel, the better. So, if we're thinking about something a little more traditional like a device-disinfection chamber, there are many principles. Although the techniques will differ, there are many principles that we can apply from how devices that are used for sterilization or chemical disinfection today are validated, in terms of what we define, what a worst-case location is may look different inside for the UVC guidance versus others. Again, going now-- This is leaping ahead to Question 2. But that list of most challenging organisms having that. And then, it's also of course typical for more traditional methods that there's kind of two pieces, and one is there's some high-level validation done by the manufacturer of the disinfection device. But then, for somebody to claim-- Then the manufacturers of the devices to be reprocessed, need to do their own work to say, “Yes, my device is suitable for this.” So, I think leveraging as much of the thought processes as we apply to sterilizers and other disinfectants is just very important for keeping that consistency and transparency as FDA referred to earlier.

00:27:00 Dr. Jarvis: Rear Admiral Peat.

00:27:02 RDML Peat: Thank you so much for the recognition. So again, this is Admiral Peat. I do have one bit of clarification for Cameron Miller. You may have mentioned that we are supposed to do testing, but the validation portion of it is not within the purview of FDA. We do look at validation testing. So, I just wanted to have a better understanding of what you had indicated regarding FDA's purview.

00:27:29 Dr. Miller: Yes, and you're right, I shouldn't speak for the FDA. I do not work for the FDA, so I appreciate you hopping in on that statement. I mean, in my mind, what would sort of revolutionize this industry is if we literally had a test where I could have a sample in the room when I apply this, and this isn't testing, this is actual application, that when I take that sample out, I could go look for my control sample before I apply the GUV. And since I, after it, have I seen three-log, four-log kill of *C. difficile*, something that looks specific to that, I know we can do that. There's been some experiments out there showing PCR testing. I could do this in a half an hour, you know, amplification. So, instead of having to wait three days for it to actually grow on a Petri dish. So, it's more of that being properly used. I mean, I can measure photons out of the device. I know I can use standards. And this was more to Question 2. ASHRAE 185.4 and HSI 2000 or more performance standards where there's a simulated room setup where the device actually has to do the work, whether one's moving or stationary or intended to use, they can show where they have deficiencies with respect to where the samples are placed. But this actual live-time knowing that it worked in the room, it's something that I just don't think exists in the market yet.

00:29:00 RDML Peat: Okay, thank you so much for that clarification. So, I just wanted to make sure that everyone on the call knew that we do look at validated tests. The methodology is what we're really trying to focus on, on a valid method for us to say whether or not the organism has a log reduction or not. So, thank you.

00:29:20 Dr. Jarvis: Dr. Arduino.

00:29:23 Dr. Arduino: Yes, this is Matt Arduino. So, I see two different things here. A chamber is a defined space, which is-- So, validation of a chamber would be much easier than a room because rooms are all different. They contain different-- Even a survey done by Bill Rutala where looking at frequently touched surfaces, items in the rooms vary across the space. The other thing here is then you have to not only look at shadowing and low penetration, but this is direct line of sight. So, beam is directional. So, part of that issue is also figuring out the

limitation is “Is the light reaching the right places or getting the right doses?” And in a room, that might be that you place dosimeters around the room that cover different areas of spaces to say, “Did we get the necessary dosage at all areas as we treated the room?”

00:30:39 And then, you have to go back then to efficacy testing and how that is set up. Because when you look at the literature and you look at people who do testing, distance from the light is another issue because a lot of the experimental designs that are not happening in the clinical-- That's a very small distance between the light and your challenge. Or that challenge is done just in liquid or on agar plates. There's no consistency as to how that's tested and defined as opposed to, you know, we have test methods for chemicals where we actually use soil and different types of carriers. And then, the product is tested that way. So, I see that there's lots of different challenges that we have to overcome here to see this. And it might be that we take representative organisms of HAI pathogens that represent general-- Everything from *Bacillus* spores, probably most likely *C. diff.* At least of those that we know may be environmentally transmitted at least by surfaces. And when you look at surfaces as a whole, it's maybe 14% to 15% of all HAIs, whereas hands and other routes are a lot higher.

00:32:23 Dr. Jarvis: Mr. Anisko?

00:32:26 Mr. Anisko Sure. Thank you and thank you guys for this discussion. This really is the heart of what we were kind of discussing earlier in terms of setting up an adequate simulated-use validation approach. We have both the chamber device, which we can agree is a much easier approach. I mean, you have a defined volume, you have a defined enclosed medical device, it's oriented a certain way. The device may have some sort of way to determine how much dose was delivered. Was it an adequate dose? And you can find a worst-case position and that validation's more straightforward I think. When you get into these room conditions like we discussed, that's a more difficult-- What does worst-case mean? And we have a lot of critical parameters that we need to address. The line of sight, the distance is a big one. What's in the room, what are the materials? And I think you guys are right. I mean, that is a challenge and

that's not always straightforward. I would say placing dosimeters around the room is something that we could look at in the validation. That definitely would be something that'd be helpful. Also, inoculation of worst-case locations and criteria such as that I think is important. And as we've discussed to date, we only have the microbial reduction claim, which is a 2-log reduction of certain surfaces. Certain materials have been tested, material comp has been tested in that regard. And as you get up into other levels of disinfection, that's where your log reduction and your panel of organisms would change. So, it's that hierarchy and it's that understanding of resistance that we try to work into it. And going forward, I think that's some of the information that might be helpful. But thank you. Thank you, everyone.

00:34:26 Dr. Jarvis: Yes, I think for me, kind of following up on what Mr. Anisko as well as Dr. Arduino said, it's easier for me to think about this in categories. One being the enclosed chamber, not open, but closed chamber and using that to disinfect, like N95 respirators, that type of thing. Second being in-room UV devices and their documentation that they can reduce microbial load. And then the third being in-room devices where there's documentation that you can reduce HAIs, which obviously is the thing we'd most like to achieve. And making performance testing the same for all of them doesn't seem to make a lot of sense to me or be practical and realistic, whereas doing it for those individual [categories] would be much easier. And the last two obviously would have a fair amount of overlap. But raising another point, which is one that one of the speakers pointed out that they were required to do testing of all these organisms that had nothing to do with healthcare-associated infections. And I do think that if you're doing testing or having criteria for either reduction of microbes in hospital settings or reducing HAIs, you really should focus on the organisms that cause HAIs and not something that you can find in the waters of Canada under UV in the air. Who cares?

00:36:19 And I think, Cameron, your group was involved in a meeting, a number of-- I think it's several years ago that's published. It has a lot of information related to these different categories and what would be useful.

00:36:39 Dr. Miller: Yes, just to briefly comment on that, like you said, one of the meetings we had, we had organizations and both of them put together-- We had 2000 different studies on different things. And the problem there I would agree is different studies. I mean, there was no standardized method on how to determine what a pathogen required to be inactivated to get that log kill or a consistent type of methodology. I had more questions for Question 2 where I thought they fit in when we get there, but that's something that we need to have in the literature is "ASTM standard blah, blah, blah" that says "This is how you measure whether it's a linear," one of those devices everybody uses on the mercury lamps to determine how much it is. But you've got to make sure there's nothing else around affecting it so we can have this hierarchy. We'll get more into that in Question 2, I think is where I see that being placed.

00:37:42 Dr. Jarvis: One other point I'd make is I think the variability in terms of infection control across hospitals is one that you have absolutely no control of. And even if I told you I do X, Y and Z, we know that if Dr. Arduino comes in and observes my people, they're not doing X, Y and Z. They're on half of X, Y and Z. And I think the only randomized control trial looking at UVGI reducing HAIs is the study out of Duke. And they acknowledged that when they did that study, by the mere fact they were doing the study, the normal cleaning and disinfection-- Or excuse me, the cleaning improved so much that it eliminated their ability to get a statistically significant result in reduction of HAIs. We're not going to have study conditions at all these hospitals, so they won't be doing cleaning as well as we would like them to do it. And so, I think it reflects the need to look at the real world and not totally base everything on an experiment in a laboratory or a multimillion-dollar study that's been done. Dr. Morgan?

00:39:02 Dr. Morgan: Yes. Are we moving on to 1b? Because we've sort of already started talking about the healthcare associated infections and I did have some thoughts on the study design that could be helpful for looking at that.

00:39:20 Dr. Jarvis: Well, why don't you hold onto that for just a minute. Let me summarize. I think where we've come with this-- And the different Panel members can raise their hands if I don't

reflect it correctly. One, the issue that there's tremendous variation in the room design and setup in healthcare facilities as well as from one type of facility to another. The issue of variability and disinfection related to cleaning and the importance of in-vitro validation, but that there's not a standard right now and you'd have to set that up. The fact that an enclosed chamber is obviously a very different world than a hospital room or operating room. That obviously one outcome could be just reduction of microbial load and the second could be decrease in HAI. And that there obviously is a great need here for standardization and there's not a lot out there in the published world or other groups that have done it. Admiral Peat, does that address 1a enough or you have other issues?

00:40:52 RDML Peat: Yes. So, thank you so much. Very helpful discussion. We're just trying to assemble the comments and thank you for the summarization. We do have a few clarifying questions. So, the question speaks to the Agency believing device innovation may support additional indications in the future such as standalone. Are the recommendations for the Panel for 1a, does that address performance testing for standalone?

00:41:28 Dr. Jarvis: Anyone has any answer to that? Dr. Morgan.

00:41:34 Dr. Morgan: Yes, Charity Morgan. I think once we got the clarification that the standalone disinfection was not meant to replace cleaning, it was just not, it would be the only method of disinfection. I think that there is a possibility that there could be innovation that would allow for standalone disinfection. And in terms of what testing would be needed for that, I think you would need to be able to compare the standalone disinfection to traditional disinfection to see that the same level of disinfection was being provided by the standalone device. So, I guess in terms of recommendation, I would say that I'm not ruling it out as a possibility. I think it would be a similar set of standards as if you were trying to justify a new method of chemical disinfection. You would compare it to an existing standard to see if they were removing the same level of microbes.

00:42:49 Dr. Jarvis: Thank you. Ms. Sauer.

00:42:53 Ms. Sauer: Yes. For Dr. Morgan, you just talked about comparative testing. Is it the same as the other? And that's certainly a keystone of the 510(k) process, but for sterilization microbial control, most of the standards just simply refer to a log reduction or getting a full kill and a partial cycle and things like that rather than-- So, could you talk a little bit more on your thought process of that need to compare versus that need to just hit an objective performance standard?

00:43:22 Dr. Morgan: Right. I didn't mean compare as in 510(k). I was including hitting an objective standard as part of comparing. So, you can be compared to the objective standard and say "Yes, you're meeting what has been already determined as 'This is the acceptable level of disinfection that we've--'" Other products or what the medical setting has said, "This is what we need for this level of device." Does the standalone disinfection meet that? Yes, it does. And that will be the level of evidence required. So, I didn't mean a comparison in terms of 510(k). I just meant in terms of [whether] you would want to have either another method or device or a standard that you were saying this standalone disinfection can measure up to.

00:44:17 Dr. Jarvis: Thank you. Dr. Miller.

00:44:20 Dr. Miller: Yes, I just wanted to clarify the statement there. So, it says the Agency's authorized general and high level disinfection and then we're talking about standalone. Are we talking about sterilization? If it's sterilization, I don't know if standalone is going to fit the bill. What's above high-level disinfection that seems to be something that's already been authorized under specific conditions? I guess I'm a little confused on the general question and what level we're talking about.

00:44:56 Dr. Segars: I'm Dr. Segars. I'd be happy to address your question and thank you for requesting that clarification. We are not discussing sterilization in the context of this question. The reference of standalone disinfection is meant more to separate from adjunctive microbicidal or microbial reduction such as that the UV technology might be the only

microbicidal process to achieve the expected level of disinfection. Does that answer your question?

00:45:31 Dr. Miller: Yes. And in this case I do believe it's possible to breach that. Yes.

00:45:41 Dr. Jarvis: Dr. Bulger.

00:45:43 Dr. Bulger: Maybe I could ask you to elaborate on a couple of things and maybe you can say in which areas you think standalone, as Dr. Segars described, might be more helpful versus whether it would be more likely that we would only see adjunctive devices. Because we've discussed the fact that UV has a different resistance pattern. There's high variability in exposure, high variability in geometry. To give you two examples, you take a spatula, you take a whisk, if you expose the spatula, the back doesn't get exposed to UV. You put it in a chamber, back and front get exposed. No matter what you do with that whisk, you have a problem. And then, the added hurdle, is that spatula being used to tuck the patient in or is it being used as a retractor to hold back tissue in an operating room? So, for us, it would be helpful, given this really helpful discussion, to say where you think, when we see the landscape of devices coming in, where standalone would be indicated; whether that's microbial reduction for a less critical device or for a level of disinfection, and remember that resistance hierarchy where we don't get fungus right away sometimes, whether it's more likely that we see standalone, or say, following environmental cleaning, whether that's always likely to be an adjunctive device for, say, devices that we use in the hospital. Would it be more likely that it would always be adjunctive and not standalone? Is that something that you can sort of give your feelings about?

00:47:31 Dr. Jarvis: Dr. Miller.

00:47:34 Dr. Miller: Yes, when I made that statement before, I was purely thinking of a chamber-type situation where the unknowns are pretty well known, that they're in a controlled environment and know what you could dose into that situation. I would even go one step further if it's standalone that the devices being put in there are compatible with the device that is meant to

be used. So, not little nooks and crannies in a device that has been designed to be UVC-disinfected at a high level.

00:48:05 Dr. Bulger: And you brought up a really important point that we talk about every day, and that's human factors testing. Because we know that manual cleaning is very labor-intensive, prone to errors as you've discussed. And then, sometimes there's the added problem that you said, Dr. Jarvis, that once people know there are robots doing automated cleaning, does that change what they do or if there are other eyes on it. So we have all that to factor into it. Human factors being a very important part of evaluating a device, whether it's a chamber or an air device or an environmental cleaning device. But we're trying to figure out where this very valuable technology is going to fit in and what the limits might be. Because we have to be the crystal ball people and see where it fits now and where it might not fit later for things we don't know about.

00:49:00 Dr. Jarvis: Dr. Morgan.

00:49:03 Dr. Morgan: To just go back to the issue of level of disinfection, I was thinking about-- In terms of the definitions that were provided in the Executive Summary about, you know, it considered what makes it low level versus intermediate level versus high level. And so, like Dr. Miller was saying, assuming that we're talking about a chamber device. So, it's designed so that the entire surface of the device is going to be hit. So, if we're thinking of spatula, we're getting the front and the back. And in order to support the indication for standalone disinfection, the device needs to be able to achieve the level of disinfection that's appropriate for the use. So, if it is a critical device, it needs to be able to be high-level disinfected when it comes out of the chamber. And then, if a device can do that, I think they've shown evidence for supporting the indication. If they can't get to high-level disinfection and it's a critical device, I think that standalone use is not appropriate.

00:50:24 Dr. Jarvis: Okay. Rear Admiral Peat, does that cover 1a?

00:50:29 RDML Peat: Yes, it did. Thank you so much for the robust discussion. The only thing that I still had a concern about as it relates to those performance testing, is there any considerations that we should have from a clinical standpoint for what studies should be conducted? I know that, Dr. Jarvis, you have really provided a wealth of information, but I haven't heard anything yet from Dr. Siddiqui.

00:51:03 Dr. Jarvis: Yes, I don't know if Dr. Siddiqui is online. He had mentioned that he might have to run to the OR so he may not be here.

00:51:12 RDML Peat: Okay, thank you so much. Thank you for 1a.

00:51:17 Dr. Jarvis: All right, if we could move on and show 1b. So, to capitulate. “In addition, manufacturers may also be interested in reducing or preventing healthcare-associated infection indications. The Agency has typically recommended a clinical study to support such indications. However, the FDA recognizes there may be challenges in designing this type of clinical studies such as inconsistent infection control practices across clinical settings, variability in reprocessing techniques, and appropriate control conditions. What recommendations does the Panel have regarding study design considerations to support indications such as the reduction or prevention of HAIs? Dr. Morgan.

00:52:13 Dr. Morgan: Okay. Charity Morgan. So, this one I think is-- This is a tricky one, I think, because we already touched on earlier the possibility of there's that little bit of an overlap and whether or not the FDA can really speak to the hospital processes that would be involved in controlling infections. And I believe it was Dr. Bulger who said that so far no one has been able to support a claim for reducing healthcare-associated infections.

00:52:51 But having said that, in terms of what study design I think would be useful for supporting a claim, I think as pragmatic a design as possible is important because we are going to have so many human factors that are going to interfere with the efficacy of these devices. As we've touched on, people are going to think, “Oh, well the robot's going to clean it so I can be a little bit faster in my manual cleaning” or “I've got a large bulk of these devices I got to get clean in

a certain amount of time, but I can be a little bit sloppier on that because I know it's going to go through the disinfector anyway." And we already know that the UV can't penetrate under through the soil or the unclean part of the device. The idea that if things are in shadow or not going to have full exposure to the light, they won't get the full dose of the UV. Is the user going to be adequately informed of that?

00:54:04 And so, I think we have to build in a study design that will be taking into account how people are actually going to use these devices, not these sterile, no pun intended, trial designs where everyone does everything perfectly and then when you got in the real world, that's not how it's actually used. So, I think a pragmatic design will give us a sort of real sense of how these devices will actually work in the clinical setting. And I think that in terms of the variability across clinical settings, using each setting as its own control-- So, sort of a step-wedge design where people start out without the UV device and rolling over to using it so that everyone can be used as their own control, can help account for that variability across clinical settings. And we can, or I guess the sponsor, can randomize based on academic medical centers, local smaller places, level of experience. And there's ways to sort of control for all that variability. But I think that that's sort of-- It's possible, but it's going to be a very tricky design. It's going to be something that needs a lot of ironing out. But honestly, I would be surprised because there-- The vegetable soup metaphor. There are so many factors that go into these infections. I wonder how big that effect size would be just from adding a UV device. How big the study sample size would need to be to be able to actually tease out the effect. But those are just my initial thoughts of what kind of study design would help a sponsor support that kind of indication.

00:56:08 Dr. Jarvis: Dr. Arduino.

00:56:12 Dr. Arduino: Yes. So, back in 2013, Cliff McDonald and I wrote a commentary on VHP study and looking at reducing infections in that setting. So, I look at these devices, whether you're a fogger, a UVC robot, a mister, or something for whole room decontamination, as these no-

touch devices-- We actually published this little commentary that gave a hierarchy of evidence that you would need to reduce infections. And you start where the lab demonstrates-- You get your 10^3 to 10^6 reduction of your pathogens. Then you go to in-use demonstrations where you say, “Are we reducing bioburden?” And then you have to say, “Well, can we demonstrate that in-use bioburden reduction may be clinically relevant?” And there are a whole bunch of things there. So, you're looking at terminal-only use reduction of same-room transmission, terminal and daily use, reduction in hand-contamination rates. Then you go up another level and you say, “We have to demonstrate that reduced pathogen transmission via admission, discharge, active surveillance testing and clinical incidents.” And then that proceeds even higher to go, “Are we actually reducing infections where you have careful attention to baseline infection rates, the trends?” “What is your study population?”, the sample size considerations, because a lot of these studies, in order to see changes, have to be big. So, you're either doing a group of institutions doing a time, pre-intervention, post-intervention sort of studies. And then the other components here have to do with infection-prevention practices that are actually-- And the components: hand hygiene, source control, isolation and device procedure and specific measures, and antibiotic use. All these have to come into play and I don't think we've even reached that level of being able to do that currently. So, where we are now is “Can we demonstrate a bioburden reduction?” And there the challenge is “Are we using the appropriate sample methods in a use-setting to demonstrate that bioburden reduction?” Because most of the time you just say, “Oh, we collected five samples with a swab.” Well, are those five samples representative of the hospital bed, or the rails or other devices in the room? And how many samples would you actually need to take to get a representative? So, where we've done some of these studies in looking at hospital rooms daily clean versus terminal clean is we ended up doing sponge samples because you can sample larger surface areas. And then you do composite sampling where you use your sponge to collect a couple of different items within the room and pull those. And then you look at log recovery before and after your treatment to

see what happened there. Another alternative would be, in some of these situations, would be to use inoculated coupons that you place around the room, and then go do the recovery of organisms from those coupons. And I think Bill Rutala has done some of these things where he had inoculated surfaces that he put around the room and then looked at the log reduction from what was basically control versus the irradiated samples. But I think to go up the chain to get to that fifth level is difficult. And I'm not sure whether it's actually-- Is it really doable? I don't know.

01:01:00 Dr. Jarvis: Yes. I guess, Dr. Arduino, one of the questions I would have is there a way for FDA to kind of stratify the different products that are out there? Almost every one of them says they can reduce the microbial burden. And then they extrapolate from that and say when they have no evidence in many cases that we can reduce HAIs. And if all you do is have that lower level of reducing microbes, then all the devices end up being the same when they're probably not. And the question then to FDA is how do you set that next level up? And I would agree with Dr. Morgan that [said that] if you're going to wait around for large randomized controlled trials, which I agree with Dr. Arduino, that is the best data you can try to get, they're probably not going to happen. The Duke study costs what, Dr. Arduino? Somewhere between 1 and 2 million dollars.

01:02:08 Dr. Arduino: Yes. It was not cheap.

01:02:11 Dr. Jarvis: And they did not-- And I think it went on for almost two years. They only studied really one device, so it wasn't even four different devices to see if there are differences. And it got blown out of the water because the study being funded meant they had better infection control practices. And so, the baseline went down and they couldn't find a difference. You're not going to get 20 more of those studies. In the current environment, you'll be lucky if you get any more of those studies. So then, I think you do fall back on the pragmatic, if I can show in my hospital that it reduces the bioburden and even more importantly the HAI rate, that should be of some importance. Dr. Miller.

01:03:04 Dr. Miller: I think this is one case where we kind of have to split it up between surfaces and the air. Surfaces, just like everybody was describing here-- And I'm speaking outside of the scope of my knowledge. So, this is getting into a little bit of just my scientific conjecture. I don't know where the infecting pathogens are coming from. I've heard different things. I've read different things. How much of what we see as statistics really comes from the bed rail, the bathroom, or other areas where we transfer? Now, in air, I think it's a completely different story. And I think there have been enough studies. Studies shown out there with tuberculosis and other things where upper room environments made differences, significant differences. So, if we're talking about air devices or airborne pathogens, I think there's opportunity to demonstrate this. I don't know if statistically it's been done, I don't believe it has been statistically done, but surfaces-- You got to first convince me where the pathogens are coming from, and are we going after the right place? A little bit of scientific conjecture there. I just want to make that clause in there.

01:04:24 Dr. Jarvis: Yes, I think certainly from the point of traditional HAIs, so surgical site infections, ventilator-associated pneumonia, catheter-associated UTIs, catheter-associated bloodstream infections, virtually none of those (with the possible exception of ventilator-associated pneumonia and even there probably not) related to air. So, I don't know that I wouldn't consider in-room devices that are killing organisms on surfaces. Very different from air purifying devices that probably for most HAIs have no relevance whatsoever. Dr. Arduino, you have any comments on that?

01:05:14 Dr. Arduino: Yes, I think when we look at where we're seeing infections, there are only certain times when we see a prior room occupant being an issue. We do know that there are issues around sinks and splash, but I think a big portion when we see transmission has to do with healthcare workers and their practices and whether, “Hey, are we actually gloving? Or are we touching a contaminated surface-- Like, I'm doing something around the sink and then going to touch a patient or do something with the patient.” So, we see with some of the outbreaks

involving carbapenem-resistant organisms, the source of those organisms is the sink drain in many times. And then you go walk into a facility and what do you see stored around the sink? Clean supplies, medication vials and other things that we keep saying, “Oh, no, no, move that away.” The other thing-- And this goes back to my training under Marty Ferrero when I first came here. Presence of a pathogen does not always equal risk. There has to be some way from that pathogen to get from wherever it is to the susceptible host. And most often, that's through contamination of the healthcare worker. And probably hand hygiene plays a role in that too.

01:07:11 Dr. Jarvis: Ms. Sauer.

01:07:14 Ms. Sauer: Thank you. This is Nancy Sauer. Dr. Arduino just raised, I think, a very interesting topic here regarding what is the source of some of these infections and it's not maybe another medical device, it's a piece of the hospital infrastructure. And I think it would be helpful to companies who are considering entering the space, doing innovation in the space, to understand FDA's position on if you say “We're going to place this over your known germ laden sink and we're going to reduce what's in that sink” and they do not go on to make claims about infection reduction, is this in fact an FDA-regulated medical device or is this more of an OSHA-style environmental control for a workplace hazard? So, I think that's just a really interesting thought and some clarity on that would certainly be aligned with some of the questions that came in via comments submitted ahead of the meeting.

01:08:26 Dr. Jarvis: Ms. Dunn.

01:08:29 Ms. Dunn: Hello, can you hear me?

01:08:31 Dr. Jarvis: Yes. Whoops. You just went away.

01:08:38 Ms. Dunn: Oh.

01:08:40 Dr. Jarvis: There you go.

01:08:40 Ms. Dunn: There I am. Okay. Hi, I'm Deborah Dunn and I am the Patient Representative. My question, a statement question just for clarification. I am a lay person. I am a patient who suffered a severe infection during a heart device switch out and the infection went to my heart.

And so I had to have lead extraction and device extraction, and it was quite a nightmare. But I'm here to try to do some good work because of it many, many years later.

01:09:14 I sat on a Sterilization Panel for the FDA several years ago. It wasn't that long ago, but it was quite enlightening and we went very much in depth as far as cleaning endoscopes and some of these devices that we're talking about today. And we had a fabulous presentation from the Nurses Association, who the nurses, from what I learned, are pretty much in charge of cleaning a lot of these devices right outside the procedure rooms and how taxing it is on their bodies. They stand on their feet. A lot of these devices are very complex with bends and twists and kind of grooves, cameras. And so, we spent a lot of time discussing this process. A little sad to hear that it probably hasn't evolved a whole lot from that time because there really wasn't another alternative. And so, my question that I have is we're talking about everything has to be cleaned, sterilized pretty much by hand, if I understand, chemically first to get past that layer. And then, if we are able to use the robotics, I assume they're expensive. And I know we don't discuss cost, but there was some talk about maybe some resistance from hospital systems because of the cost of that second tier. And the FDA may be able to put something into play to help subsidize that. So, my question is going a little bit more in that direction because we're talking a lot about the robots. What is the likelihood of hospitals being able to afford these and how many would they be able to afford? And is there something in the pipeline to help with credits for them to incentivize this? Thank you.

01:11:22 Dr. Jarvis: Anyone from FDA want to address that?

01:11:31 RDML Peat: Thank you so much, Ms. Dunn, for that question as well as the commentary. We agree with you in many instances, but within FDA, our purview is not necessarily focused heavily on finances. One of the things that we do is work very closely with our reimbursement arm, which is the center for, CMS. And within that particular group, there is an opportunity for sponsors to come in with a parallel review of both FDA and CMS to be able to move forward very quickly on our patients having access to these devices, but at a reimbursable cost. That

would be something we'll take under advisement in moving forward as we think about it a little bit more. But our focus would be heavily on the regulatory side of it to be able to address safety and effectiveness of the device. Hope that helps.

01:12:33 Dr. Jarvis: Great. Thank you. Dr. Arduino.

01:12:36 Dr. Arduino: Yes. So, it's not only purchasing devices like this. So, there's a local hospital that purchased 12 of these devices. Are they in use? No, they're in the basement because they do not have the staff to operate them. So, the other issue we're facing here is staffing issues, especially among EVS workers, many of whom are contract services and not hospital employees. So, there's a workforce issue around some of this as well.

01:13:23 Dr. Jarvis: Any other comments or questions related to 1b? If not, one of the things I forgot to mention when I was saying if you have some kind of validation process that involves killing the organisms to have the organisms that are prevalent in hospital infections, I would include as a subset and an important part of that to make sure you select some of the important multi-drug resistant organisms such that have been mentioned; MRSA has been mentioned, carbapenem-resistant organisms have been mentioned, *C. difficile*. So, to summarize, concerned about the various studies and the difficulties of doing an appropriate study, documenting that in-room UVGI devices can reduce healthcare-associated infections. But nevertheless, the importance of having such data, including well-designed studies, but also pragmatic-design studies that smaller hospitals or non-academic centers or with the lack of funding might be able to do particularly before or after observational studies-- The importance of-- If you're doing a comparative study using a similar location in the hospital or surgery center as a control, showing that the devices can reduce the bioburden in use in a practical setting, show the clinical relevance of this, use the correct methodology, whether we're talking about a microbiology methodology or the clinical design of the study. Could use something like inoculating coupons, which are used for the chemical disinfectants, but do it for UVGI. The issue of surface organisms versus air organisms. An important issue of trying to

incentivize and, as Rear Admiral Peat mentioned, that could be done through CMS, there's no doubt if you want something done in a U.S. hospital, the way to do it is have CMS link it to payment and it will be done. Nothing that any of us say we'll get done unless they want to do it. And the issue of such as using a UV device over a sink of whether it becomes an OSHA issue or really an FDA issue. Dr. Peat, does that answer 1b well enough or there are other issues you'd like us to address?

01:16:47 RDML Peat: Yes. Thank you so much, Dr. Jarvis. That answers 1b quite excellent. One of the things that I love hearing from the rich discussion that was had by the panelists is the fact that FDA still always grapples with these study designs. So, it's great to hear some of the conversation that correlates with the thoughts that we're having internally. So, thank you.

01:17:10 Dr. Jarvis: Super. If we could get question number two. So, to recapitulate: "To support appropriate performance testing, the Agency currently asks manufacturers to determine an appropriate hierarchy of microbial resistance to germicidal UV for reprocessing of medical devices. To avoid development of a level of evidence that may be specific to individual UV devices, FDA is seeking recommendations on a scientifically justified consensus for level of evidence that should be established for germicidal UV hierarchy that could be applied across the device type without individual manufacturers developing new hierarchy testing for each new device." And "Does the Panel have recommendations on what information would be needed to support a general hierarchy of resistance to UV?" Ms. Dunn.

01:18:17 Ms. Dunn: I'm sorry, I did not realize my hand was up. I don't have a question.

01:18:21 Dr. Jarvis: Okay. Dr. Miller.

01:18:26 Dr. Miller: I think, like I said, I can show you to the paper on the NIST Journal of Research that this compilation-- I mean, there are thousands of studies out there, but they all had their own idiosyncrasies and me, even though I'm not a biological person, could pick out some of the problems that some of them may have had. We need a standardized methodology for determining-- And what I would say is just the baseline pathogen itself, making sure that

there's nothing around that can cause some secondary effect where I'm photoionizing something that actually then kills or inactivates the pathogen as opposed to just the pathogen itself. If you had this process, I know the IUVA was even looking into coming up with something like this and doing a round robin amongst people that do this type of experiments to see how consistently they come up with the K rate. If you had something like that, then you had at least a starting point of understanding a hierarchy. It's going to be a fuzzy line no matter what, but it's going to be at least a hierarchy that we could then say, "If you can pass this pathogen, you're probably going to catch this group;" "if you can get this one, you're going to get that group;" "if you're getting *C. difficile* or some spores up here, wow, you're really hitting it pretty hard type of thing." So, somewhere that we come up with this standardized methodology. Now, that's when it really gets into the application, then is how well do I get the optical radiation there, and what is it on the media? There was a good shown picture earlier in the commercial products where they showed the angle of incidents plus the valley structure on some of these materials. Rooms could be designed better or products could be designed better to accept UV disinfection, which is something of a whole give-and-take between the systems of applying it, and then being ready to use the UV when it gets there, the photons over.

01:20:36 Dr. Jarvis: Ms. Sauer.

01:20:39 Ms. Sauer: Yes, so speaking for industry, very much welcome. A standardized consistent approach and whether OSEL or some others can help with building this out. A couple thoughts just on some of the how. Seems like a very good place to start is with just a base understanding of the biology of the organisms and spores that we're concerned about. Let's build some categories that way, but not an excessive number of categories. I would hate to see this suddenly have 20 categories where we really only think about five when we're talking about a chemical. So again, some of that consistency across methods, but let's start, it seems, with the basic biology and then write some candidate organisms within those major categories. I saw pigmented spores show up in the materials. That makes a lot of sense, right? A spore is

inherently hard to kill, that is its job. Okay, now we add pigment in. Yes, it makes sense that that would be-- So, okay, there's a group, now how can we go about identifying at least the most, maybe not obviously single, the most challenging, but here's a good representative. But yes, it really is essential that this basic science not be handed over or put on the back of every manufacturer who wants to develop a device in this space.

01:22:22 Dr. Jarvis: Dr. Arduino, do you have any comments on this?

01:22:29 Dr. Arduino: And I agree with Cameron. This goes back to doing some round robin research. Even when we did do methods with EPA, they usually pull a round robin of different laboratories to make sure we all come up with the same answer or close to the same answer. The other thing I think you have to look at and say, "Okay, what are our challenge organisms?" I just reviewed a paper for a journal where they were talking about using UVC for sterilization. So, they developed the *Bacillus atrophaeus* biological indicator to be used this way. Their study was flawed on several fronts because what they found was that it all depended on time. And even then, they never did get the total kill of spores. And they only ran their experiments out to 12 minutes. So, they measured at one minute, they measured at two, and I'm sitting there going-- And the variability even within the sport preps was variable. And so, in their discussion they talk about disinfection, but they didn't really talk about-- And again, their test method, again, used inoculated agar plates, which I don't think is a way to-- Just like people who do testing in water. Well, that's okay for water disinfection maybe, where you have your agent in a water-based solution, but that doesn't carry across the board. So, I think we need to really look at a standardized protocol that everybody can use and agree upon. And whether we use *C. diff*, we use a mycobacteria, we use maybe a *Bacillus atrophaeus*, and then we look at some of our gram-negatives and maybe an *Aspergillus* and a *Candida auris*, and see what happens. But we have to use the same method of testing in the addition with and without maybe organic soil. Just to see how that comes out. Again, we're looking at maybe approaching the same labs that do testing for chemical disinfectants and asking them to say,

"Would you be willing to do this sort of thing?" And then, defining what is the most accurate distance between the light and your target should be.

01:25:47 Dr. Jarvis: Great. Thank you. Dr. Miller.

01:25:51 Dr. Miller: Yes, I would-- To clarify more that-- I agree with you. We measure, I hate the term, but the dose. How many millijoules per square centimeter did I hit them with, right? Independent of distance and everything, that's the content of how many photons got there. And I would agree that maybe the water stuff would give us a baseline of how many photons does it take to knock out the pathogen and then go with the engineering approach of, "Okay, now I've added soiling, which I know has an absorptive property that's six times what the cell or the pathogen is. So, now I get up my number by six, what other things are going on?" I'm coming in at different angles thrown by that example. Now, I'm going to need twice as much coming in at 45 than I am at directly on, so I need to up my tolerance again. So, knowing what you're going after from the engineering approach would allow this growth. But then all once again is getting back to the application. And that's what I sort of want to divide out. There's knowing how many photons I need to take out the pathogen, and then where the product lines that I've seen have shown the true innovation is how they get those photons there. Wheeling one device in with a lamp does something, but when they start moving around and they start having multiple ones that the irradiance, but it's the energetic, the fluence, the spherical ratings is the actual term gets there. That's what we need to know. But it would be nice to have a hierarchy of just how susceptible individual pathogens are and then we engineer on what happens to our photons that die before they get there to the pathogen.

01:27:38 Dr. Jarvis: Dr. Miller, a question on that paper from that symposium that you all had. I'm not finding it on my paper here, but there was one chapter that was written that literally is page after page, after page, after page of tables trying to at least start the development of a hierarchy. And it seemed like that to me would've been a very good starting point for the FDA to look at. And then, one of the things that just lists microorganisms would be to separate it

into organisms that are prominent in healthcare-associated infections versus environmental. Because obviously if you're using an in-room device, your primary purpose is to kill the organisms that are associated with healthcare-associated infections. Whereas if you were using an enclosed device for disinfection of medical devices or personal protective equipment, you might be a little bit more concerned about environmental organisms. But it seems like there's a lot of data out there. They may not have used all the same methods, but at least gives you a ballpark of where to start.

01:29:05 Dr. Miller: Yes, I'm trying to find the link and I'll put it in the chat to the FDA folks.

01:29:10 Dr. Jarvis: That'd be great. Anything else on Question 2? So, we've talked about the importance of starting with the baseline pathogen characteristics, standardizing consistent process, maybe dividing organisms into several categories rather than one through five million, perhaps funding studies to perform standardized method or methods and using a round robin approach, ensuring that you have the correct microbiologic methods and designs of the studies, a standardized protocol, and selecting organisms that are either environmental or HAI-associated. And then, as Dr. Cameron mentioned, having-- And I think this paper does include it, the fluence, millijoules per centimeter square, that's listed in that paper for all these hundreds of organisms. Rear Admiral Peat, is there anything else that we need to cover?

01:30:36 RDML Peat: No, thank you. This is adequate, extremely helpful. Thank you for the rich discussion.

01:30:42 Dr. Jarvis: If we could get question number three. So, question number three is “With increasing use of germicidal UV devices to reprocess medical devices in clinical settings, as with frequently used antimicrobial agent, increased antimicrobial resistance is a major public health consideration. As it relates to UV safety and effectiveness of medical devices, what susceptibility testing, exposure limits and/or review aspects should be considered to support antimicrobial stewardship to guard against potential emergence of UV resistance among clinically relevant microorganisms? Does the Panel have suggestions on ways UV devices

could be used in conjunction with existing practices that would help mitigate the rise of UV resistance?" Comments? Dr. Morgan.

01:31:46 Dr. Morgan: Yes. This is more of a question. I don't know how possible it is for these devices to tell the user if an insufficient dose has been delivered. As I understand it, the concern is that some of these pathogens might receive some UV exposure but not enough to eliminate them. And that could lead to resistance. And if there's a way for these devices to give off a warning saying "It wasn't in use long enough, we turned it off too soon," so that the user can be more aware that the risk is there for UV resistance. I think that could help with the stewardship. But beyond that, I don't know how much this is really the scope of these devices. I think, is this really safety and effectiveness of the device? I know it is a very important public health question. I just don't know how it fits into what the mission is here.

01:33:27 Dr. Jarvis: Thank you. Dr. Miller.

01:33:31 Dr. Miller: I have a question to answer the question. So, how do the chemical folks mitigate this situation? Maybe that's more to the FDA.

01:33:56 Dr. Jarvis: Anyone from the FDA want to address that?

01:34:01 Dr. Xue: I can have some comments. So, basically the antimicrobial resistance-- The idea came from the drug use as some antibiotics use. If you use the last dose that's high enough to kill the bacteria and you continue to use that, that will cause the problem, antimicrobial resistance. I think when talking about drugs, this has been studied very well about this topic, but since the UV technology is relatively new, I don't think there are a lot of studies on this topic. So, that's why we just research the questions to seek your feedback or suggestions. Do you think that's a problem or do you know any studies that can mitigate this risk?

01:35:05 Dr. Jarvis: Dr. Arduino.

01:35:06 Dr. Miller: I know it's a question. Yes.

01:35:08 Dr. Arduino: So, looking at chemical disinfectants and resistance, everybody publishes it about quaternary ammonium compounds and how they may select for a drug resistance. And when

you actually look at the studies, it's more-- They develop tolerance. And this all has to do with efflux pumps and it's always to concentrations below the concentration, the use concentration of the product. But it's still an area that people do a lot of looking at. And we do know that there are organisms, like those in the *Burkholderia cepacia* complex and some of these other gram-negatives that have contaminated these products. So, commercial antiseptics and some in the way of disinfectants, when you look at iodophores at the plant where they were being made, there were issues with biofilms present.

01:36:39 Dr. Jarvis: Question for the Panel. To my knowledge, UV devices do not cause antibiotic resistance. And I think this statement to me would cause a lot of confusion out in a clinical setting to lead people to believe something occurs that I'm not aware of ever occurring. And in fact, the one in the Executive Summary that was raised had nothing to do with UV devices. It was in some way far North where the lake is frozen most of the time, and they were talking about UV-B and -C being involved and it still had nothing to do with antibiotic resistance. So, I guess my first question is does the FDA really want us to discuss antibiotic resistance or are you concerned about UV resistance?

01:37:45 Dr. Xue: I think it should be about UV resistance, not really the drug. The antibiotic resistance is another topic.

01:37:54 Dr. Jarvis: Okay. Thank you. Ms. Sauer.

01:37:59 Ms. Sauer: Thank you. Nancy Sauer here, the Industry Representative. I guess I want to just echo what I heard, particularly from Dr. Morgan. This is getting kind of broad and deep and really has so much to do with the whole ecosystem in healthcare facilities. A lot of the practices there, I think this is getting to be a lot to ask a medical device manufacturer to solve this long-term problem that we're still not sure if it exists or not. So, I think we need to be a little cautious about how this would make its way into any guidance or regulation.

01:38:48 Dr. Jarvis: Dr. Arduino.

01:38:52 Dr. Arduino: So, in the dialysis setting where UV devices are used in their water treatment systems, they are equipped with audible and visual alarms to let you know when the lamps finally reached their effectiveness. Because we have seen some of the gram-negatives in these systems develop tolerance to UV. So, you want to make sure that the lifespan of your lamp is appropriately monitored, but these aren't going-- I don't think they really have-- This is more of a functionality of the device and whether the device is equipped with a timer for how many hours that lamp has been in service. But I don't think it's going to, again, it's all about tolerance to the UV-C and not really about antimicrobial resistance.

01:40:10 Dr. Jarvis: Thank you. Dr. Miller.

01:40:14 Dr. Miller: I mean, I think in this case-- People have asked this question a lot and the only thing that sort of comes to mind is somehow the pathogen has, through random luck, or taught itself, to develop UVC-absorbing molecules that it puts in its shell, that keeps the UV photons from getting to its core, the DNA, which is what we want to do. You're not going to change the absorption curve DNA without changing DNA. So, it's more of a monitoring system. If UV systems were to go in all wild everywhere, once again, going back to this standard practice of determining what the K rate is for a log kill in water, we'd have to watch over the years saying, “My gosh. This is twice what it used to be, what's going on here?” So, it's more of a monitoring process if this actually becomes a significant commercial and effective enterprise. I don't think there's much you can do with the-- It's more evolutionary than it is at the time. It's not quite like the microbial concept because I think the devices, I mean, the path devices, the pathogens would have to change as opposed to just picking out the ones that have already evolved that way.

01:41:41 Dr. Jarvis: Anything else on 3? So, question about whether the devices measure the dose and whether it's adequate or not. I think some do, some don't, as far as I know. To be cautious about including this as a requirement for manufacturers, since it really is more UV-C resistance than antimicrobial resistance, that it might be best monitored or assessed through a

monitoring process. And last, that it may be more related to insufficient dose or inadequate monitoring of how long the lamp has actually been used. Rear Admiral Peat, does that cover everything you need on number three?

01:42:44 RDML Peat: Yes, it does. Thank you so much, Dr. Jarvis. This is an adequate response. Thank you.

01:42:49 Dr. Jarvis: Right. If we could get question number four please. So, "During the COVID-19 public health emergency, certain emergency use authorizations utilized UV as the primary microbiologic agent, such as UV decontamination systems used to reprocess personal protective equipment. In addition, the Agency has seen an increase in innovation related to UV technologies as a mode of disinfection for medical devices. Increased innovation could lead to confusion regarding how such products fit within the overall landscape of devices intended for infection control. What information is helpful to healthcare providers to promote transparency and improve comprehension for the intended uses for which these technologies are currently authorized?"

01:43:56 I might start. I think one thing is that maybe dividing these devices into categories, such as chambers for disinfection of medical equipment versus reducing pathogen loads in the environment versus reducing HAIs; and helping the consumers understand the difference between those three and that they shouldn't assume if one of them is a claim that the other two probably are too. Dr. Morgan.

01:44:41 Dr. Morgan: Yes. Charity Morgan. I mean, we saw some examples of deceptive marketing during the Open Public Hearing. I think that it would be helpful for healthcare providers to hear from the FDA about what these devices can and can't do, what the limitations of the technology is, especially the parts about the low penetration. The devices need to be thoroughly cleaned before the UV device is used. That shadows and direct light. I think these are messages that could easily be lost in translation. And so, I think clear communication from

the FDA about what-- Especially since this field is moving so quickly, making sure that healthcare providers are fully informed about the limitations of these technologies.

01:45:51 Dr. Jarvis: Dr. Arduino.

01:45:54 Dr. Arduino: Not only that, but I think we should get EPA on the phone and we should all be talking the same bullet points that if the device is being used in a medical or a healthcare facility, it's FDA because the standards of EPA are a lot different because there is no efficacy testing as far as I know at EPA with these devices. They just have to be manufactured in a registered facility. But if that might help with some of the confusion, almost like we have with high-level disinfectants where EPA will say, “Go talk to FDA.” And then, maybe that would help with how these devices are marketed and how people will be looking at these devices.

01:47:01 Dr. Jarvis: Anything else, Ms. Sauer?

01:47:05 Ms. Sauer: Yes. Nancy Sauer here. Yes, I think it's something that would help, and that I don't think many manufacturers would have an issue with is a really, almost like you would have a summary of a clinical study. If this were a drug, what is the summary of your testing? What did we test? How did we test it? A little bit about those conditions would really help because yes, there are some general limitations we want to make sure if they're not overstated as innovation occurs and maybe some barriers will never go away. But maybe a device learns how to do lumens and some intelligence may come into some of these room devices so that they can ensure a more consistent delivery of dose throughout the location. So, I think let's be careful about blanket statements against, “Oh, right, they're not going to do this and they're not going to do that.” But instead ask for very proactive, and clear and objective statements of how they were tested and what was learned from that testing.

01:48:21 Dr. Jarvis: Okay. Dr. Miller, do you have anything on this?

01:48:26 Dr. Miller: I do not, on this topic.

01:48:29 Dr. Jarvis: Okay. So, in summary, it’s important to educate clinicians or users about their use. What are the benefits? What are the limitations? What different devices can and cannot

do? To coordinate with EPA part of that communication. Clarifying for all users that if it's used in a healthcare facility, FDA has authority; and if it's outside of healthcare facilities, EPA has that authority. And maybe even contrast or compare what rules or regulations-- Kind of a summary, as Ms. Sauer said, for testing what regulations one versus the other has so they realize they are very different. And then, to consider requiring a summary of the testing, whether-- Particularly if it's nonpublished. If it's published, it's easy for them to hand out a reprint. But most of the time these companies don't have published studies, but they have done internal studies and no one else knows what the data are. So, that would be very important to know. Rear Admiral Peat, did that cover this one?

01:49:55 RDML Peat: You did, Dr. Jarvis. Thank you. It's adequate.

01:49:59 Dr. Jarvis: Okay. If we could see number five, please. So, this is free for all. What other considerations for innovations in germicidal UV reprocessing of medical devices does the Panel recommend? Dr. Arduino.

01:50:38 Dr. Arduino: Maybe the development of process measures so that we know we have done what we said we were going to do, or the devices performed what they were going to do. So, people nowadays are using fluorescent markers to look at room cleaning or ATP as an evaluation of cleanliness. Is there something else that we could look at that is relatively quick to tell us that we've successfully reprocessed the device?

01:51:24 Dr. Jarvis: Yes, thank you for saying that, Dr. Arduino. That reminded me that earlier I was going to mention that if you're going to have a validation method, it really should be based on culture, not ATP or PCR testing. So, you're testing how many dead organisms you have, who cares? You want to know how many live organisms you have. So, being very cautious of manufacturers who might provide either PCR or ATP data is evidence of efficacy. Any other considerations? Dr. Miller.

01:52:04 Dr. Miller: On that note, I mean, I think there's some of these processes where you amplify-- If you're looking for a particular pathogen, that you could draw a correlation factor between

that type of testing and culture-based systems-- I wouldn't completely toss that out yet, what you had just mentioned as a potential live-- And when I say live, within half an hour turnaround time on whether you've inactivated the species that you're looking to inactivate. Just a research aspect.

01:52:46 Dr. Jarvis: Any other comments? Dr. Morgan?

01:52:54 Dr. Morgan: I don't. I feel like we've covered everything I had to say about study design.

01:53:02 Dr. Jarvis: Okay. Rear Admiral Peat, did we cover that one? We're not in an innovative mood today. We'll leave that for the manufacturers.

01:53:13 RDML Peat: Thank you so much, Dr. Jarvis, and thank you to the Panel.

01:53:26 Dr. Jarvis: At this time, I would like to ask our representatives, Ms. Rachel Brummert, our Consumer Representative; Ms. Nancy Sauer, our Industry Representative; and our Patient Representative, Ms. Deborah Dunn, if they have any additional comments.

01:53:44 Ms. Brummert: Hi, I'm here, Dr. Jarvis. We're having a windstorm and I'm trying to keep from being kicked off, so I have my video off. I do not have anything to add at this time. Everybody asked my questions already.

01:53:57 Dr. Jarvis: Great, thank you.

01:54:04 Ms. Dunn. This is Deborah Dunn and I do not have any more comments. Thank you.

01:54:08 Dr. Jarvis: Thank you. Ms. Sauer.

01:54:11 Ms. Sauer: Yes. Just thanking the FDA for bringing this together. I think this is a really tough area for everyone to navigate right now. And so, very honored to have been a piece of this. And just kind of with regard to that last question, recommendations, expect innovation. I think there's going to be-- Not that I know of anything specific, but I anticipate that there will be some very interesting approaches to improve the efficacy and flexibility of this. So, I hope FDA keeps their framework open to that with that in mind.

01:54:49 Dr. Jarvis: Great. Thank you all. At this time, the Panel will hear some comments or clarifications from FDA.

01:54:57 RDML Peat: Well, thank you so much, Dr. Jarvis, and to all members of the Panel for your valuable participation today at CDRH, General Hospital and Personal Use Devices Advisory Committee Meeting. I know this is a very challenging topic and we really wanted to bring this particular topic to the group as it was focused on germicidal UV technology for medical device infections. I can honestly tell you that your insights and expertise contributed significantly to our understanding of stakeholder perspective on UV germicidal disinfection technology, and the concerns that we have with implementation and challenges, the performance testing methodologies, and the views expressed on the standards for evaluating UV-germicidal device efficiency, study design considerations that will lend itself to future regulatory actions. Now, the recommendation that you have provided today by the Panel-- This information was useful in informing FDA's approach to improving our total product lifecycle evaluation framework for UV germicidal devices. And we wanted to lastly just express our thanks. We appreciate your commitment to advance in safe and effective medical device technologies. And we do look forward to continued collaborations as we develop a comprehensive documentation. And I won't necessarily say what that documentation would be for germicidal-UV disinfection devices. But the information provided today was a wealth of information that we'll utilize in moving forward. Thank you.

Adjournment

01:56:40 Dr. Jarvis: Great. Thank you. I would like to thank the Panel, FDA, the invited speakers and the Open Public Hearing speakers for their contributions to today's Panel meeting. I especially want to thank Ms. Washington for all the work and helping to coordinate this from our side and the meeting of the General Hospital and Personal Use Devices Panel is now adjourned. Thank you all very much for your participation.