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Advances in Sterilization

NEWS AND OPINION IN THE ADOPTION OF NEW-GENERATION STERILIZATION TECHNOLOGY

Instrument Sterilization and the FDA: Facts You Should Know

FDA Regulation of Sterilization Systems

Sterilization has been used in various forms to achieve asepsis in medical practice for more than a century. Yet, not until 1993 did the United States Food and Drug Administration (FDA) issue the first 510(k) marketing clearance for a general purpose medical sterilization technology. (A liquid-based sterilizer for use in hospitals to sterilize immersible endoscopes and microsurgical instruments was cleared in 1988.) These new technologies were the first sterilization systems for use in hospitals to be subject to FDA requirements for premarket notification and review under the 1976 Medical Device Amendments.

Under the Federal Food, Drug, and Cosmetic Act (FFDCA), device manufacturers must ensure that the product they intend to introduce into interstate commerce is safe and effective for its intended use. Since provisions requiring premarketing notification to the FDA for new devices were not enacted until the Medical Device Amendments to the FFDCA in 1976, sterilizers that use technologies introduced before 1976 have not been subject to the extensive review that is part of the premarketing notification process.

Traditional sterilization systems, including steam and ethylene oxide (EtO) marketed prior to 1976, fall into this preamendment category, while new sterilization technologies are subject to general and special controls as defined in the Act.

FDA Requirements for New Sterilization Technologies

A manufacturer intending to market a new sterilizer for use in a healthcare facility must file a premarket notification [510(k)] submission to the FDA for clearance to introduce the device into interstate commerce. In a March 1993 guidance document on premarket notification submissions for sterilizers, the FDA recognized that, "Sterilizer technology is expanding at an accelerating pace. Sterilizers can be complex in design and methods of sterilization are diverse. In spite of the complexity and diversity, there are some common considerations that can be applied to virtually all 510(k) submissions for sterilizers."

Specifically, the FDA requires manufacturers to provide data on the ability of the sterilizer to destroy a broad range of microorganisms. After determining the organism most resistant to the sterilization process (usually bacterial spores), the efficacy of the system must be validated. For validation, the FDA requires the manufacturer to demonstrate that the probability of spores surviving after the sterilization process is no greater than one in one million. These results must be achieved on a broad variety of instruments that are representative of actual hospital usage, in one-half the time of a normal sterilization cycle.

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The FDA will not grant clearance to market a new sterilization technology unless the manufacturer provides a validated, reliable biological indicator for routine efficacy testing based on a resistant, reproducible, and commercially available organism. In addition, documentation of system software and functions must be provided to show that the system will perform reliably and, if

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needed, detect and alert users of failures in performance.

Finally, a variety of tests must be conducted to ensure the safety of the system for healthcare professionals and patients. Examples include tests to determine the potential toxicity of any residuals that may be left on instruments following the sterilization process, and biocompatibility tests to study possible adverse health effects for workers and patients. Materials and device compatibility tests also must be conducted to evaluate the potential for materials degradation and to show that the functionality of devices is not impaired following the sterilization process. ❖

Publications Explore Issues in Sterilization

Sterilization is an important technological component in the success of virtually all diagnostic and surgical procedures. With advances in medical instruments and devices, however, the field of sterilization has become increasingly complex, leading to serious interrelated safety, economic, and environmental concerns about traditional low-temperature sterilization technologies. The recent introduction of novel low-temperature sterilization technologies that have been specifically designed to address these concerns now may make it possible to better protect healthcare employees, patients, and the environment, in a cost-effective manner.

Communicore has published a White Paper, *The Future of Low-Temperature Sterilization Technology: Safety, Economics, and the Environment*, and *The Future of Low-Temperature Sterilization Technology In Healthcare, A Roundtable Discussion*, that address these concerns. To receive complimentary copies of either or both of these publications, please complete and mail the attached BRC, or write or fax Communicore, 220 Newport Center Drive, Suite 8, Newport Beach, CA 92660. (Fax) 714/644–7406. E-mail address—admin@communicore.com ❖

Manufacturers' Promotion of "Off-Label" Uses: Are You at Risk?

After a manufacturer has met the United States Food and Drug Administration (FDA) requirements for sterilizer validation (see related article on page 1), the agency grants the company clearance to market the product based on the uses which the manufacturer has qualified. The uses that are cleared by the FDA sometimes are referred to as "labeled" uses because they appear in the product's labeling. Uses that are not cleared, therefore, often are termed "unlabeled," or "off-label."

Under the Federal Food, Drug, and Cosmetic Act (FFDCA), the manufacturer has a legal responsibility to avoid making any false or misleading representations about a product's intended uses. The company also must refrain from promoting "off-label" uses of cleared devices—a practice that may result in civil and criminal penalties, including product seizure, injunction, or prosecution.

While federal laws do not prohibit physicians from using cleared products for unapproved uses, the FDA observed in a *Federal Register* notice (November 18, 1994) that "...manufacturers' promotion of such unapproved uses encourage[s] physicians to extend the use of the device beyond that which has been proven to be safe and effective." In addition, the agency notes that, "If a manufacturer were free to promote its product for any use, the manufacturer would have little or no incentive to conduct the necessary clinical trials to demonstrate that the product is safe and effective for its intended uses. As a result, consumers would be exposed to products whose safety and effectiveness for the unapproved uses are unknown. In addition, consumers and healthcare professionals may avoid or delay using known, effective therapies or products as a result of the attention given to unapproved uses."

In an interview with *Advances in Sterilization*, **R. Stephen Trosty, J.D., M.H.A.,** a past president of the American Society of Healthcare Risk Management, said that healthcare providers need to be aware of the implications of off-label use. *"Healthcare institutions that implement unapproved uses of medical devices may face product warranty cancellation, product liability lawsuits, or malpractice lawsuits, all of which have major cost implications."*

Trosty noted that at the most basic level, the manufacturer has the right to cancel the warranty and refuse to repair or replace a device if a healthcare provider uses it in a way other than intended or "labeled." More importantly, however, the institution that allows off-label use is vulnerable in the event of legal action. In a product liability lawsuit, the institution or healthcare provider may claim that a product is defective; however, if the manufacturer can prove that the intended use of the product was altered, the institution may not have legal grounds for a claim.

Similarly, the healthcare provider and institution may face severe consequences in the event of a malpractice lawsuit if it can be shown that a product was used for a purpose other than the manufacturer intended (or

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The Bell Tolls: CFCs Are Gone, But Regulations Linger

As of January 1, 1996, the United States Environmental Protection Agency (EPA) deadline for the elimination of chlorofluorocarbons (CFCs) that destroy the Earth's ozone layer (see *Advances in Sterilization*, Vol. 1, No. 1) has officially passed. By now, most hospitals have sought an alternative to the "88/12" sterilization systems that use a combination of ethylene oxide (EtO) diluted with CFCs. Mixing the EtO sterilant with CFCs reduced the flammability of the gas and was less expensive than using pure EtO.

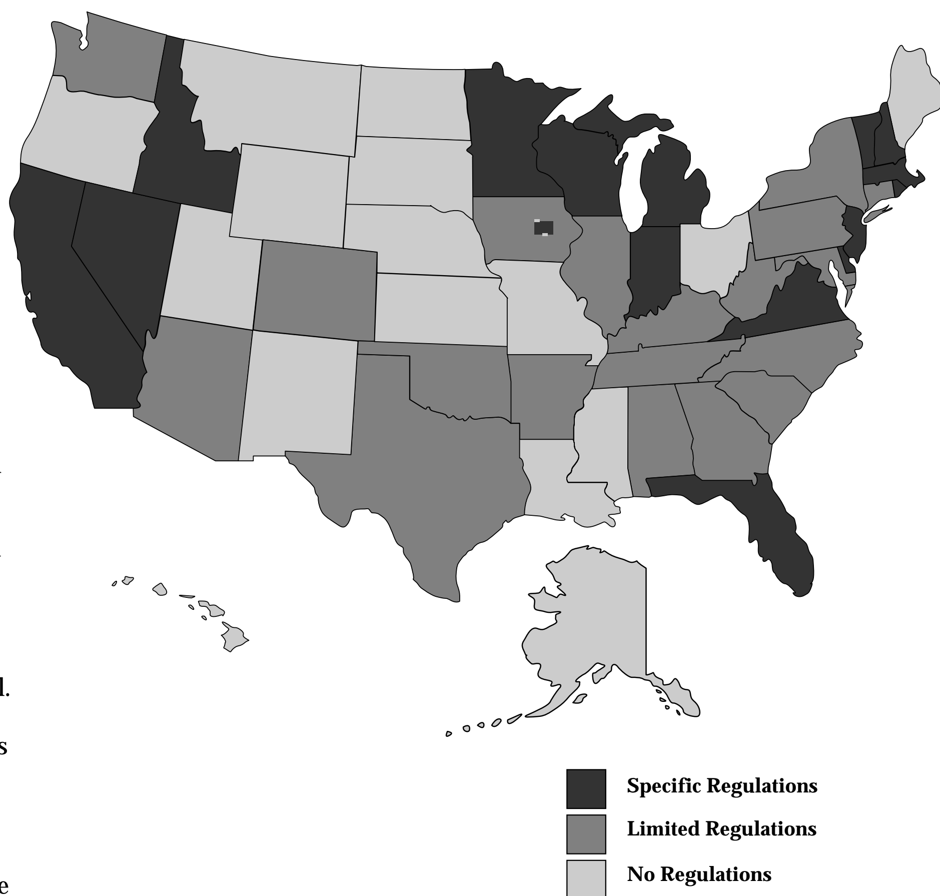
Some hospitals have chosen to retrofit their existing sterilizers to use hydrochlorofluorocarbons (HCFCs), a less environmentally dangerous form of CFCs, while others have switched to 100% EtO systems. Other institutions have been able to eliminate or significantly reduce their use of EtO with new sterilization technologies that do not use EtO or HCFCs.

Facilities using new sterilization technologies may be able to circumvent increasing restrictions governing the use of HCFCs and EtO. Like CFCs, HCFCs are scheduled to be eliminated under the provisions of the Clean Air Act. The official deadline stands at December 31, 2030; however, the government-mandated phase-out requires institutions to reduce the use of HCFCs by 99.5% by the year 2020. Until then, hospitals can expect to pay increasingly higher taxes for HCFC use. In Europe, the European Parliament has motioned to advance the date for the worldwide elimination of HCFCs from 2015 to 2003. If the Parliament is successful, the deadline in the United States may be revised as well.

In addition to its regulation of CFCs and HCFCs, the EPA is required to regulate EtO, one of the hazardous air pollutants (HAPs) listed under the Clean Air Act. Last year, the agency issued its final air toxics rule for controlling ethylene oxide emissions, requiring a 96% reduction in EtO emissions from commercial operations and contract sterilization sites. While the rule does not directly affect hospitals, it supports the increased scrutiny of EtO at the state and local level. These agencies are increasingly requiring abatement of EtO emissions to meet ambient air quality standards as defined by the Clean Air Act or by state laws (see map).

For example, the California Air Resources Board requires all hospitals using more than 25 pounds of EtO per year to install devices to control 95–99.9% of sterilization and aeration emissions, depending on the total pounds of EtO used per year. Local agencies in California have the option to create more stringent EtO controls. California's Bay Area Air Quality Management District has created rules based on the size of the sterilization chamber, rather than the quantity of EtO used. The district requires 99% of sterilization emissions to be controlled for sterilizers with a capacity of less than 10 cubic feet. For larger sterilizers, 99.9% of emissions from the sterilization process and 95% of emissions during aeration must be controlled. Many large metropolitan areas that are not in compliance with the ozone limits set by the Clean Air Act may soon follow California's lead. ❖

EtO Emissions Restrictions by State



Manufacturers' Promotion . . .
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the FDA cleared). *"It's true that if a problem never arises, there may be no negative effect as a result of off-label use,"* Trosty observed. He added that materials managers and other healthcare providers should nevertheless be cautious if approached by a manufacturer promoting off-label uses of a sterilizer or other product.

"First, healthcare workers should notify a supervisor of the situation, then check to see if the institution has policies and procedures regarding off-label use," Trosty said. *"Finally, if possible, the healthcare professional should notify the institution's product usage and development committee for assistance in the decision on whether to implement off-label uses."*

Trosty said that full disclosure by the manufacturer about the status of the device allows healthcare professionals to make informed decisions and lessen the possibility of risk for the institution. *"It is not a decision that healthcare professionals should be making unilaterally,"* he said. ❖

NEWS BRIEFS

❖ According to a recent report by the World Meteorological Organization, the holes in the Earth's atmospheric ozone layer continue to grow. The report estimates the current size of the hole over Antarctica at approximately twice the size of the entire European continent.

❖ Occupational dermatitis and asthma related to the use of latex rubber gloves could be the result of a reaction to the ethylene oxide used to sterilize the gloves, rather than to the latex, according to study results published in *The Lancet* (November 25, 1995). The authors found that "traces of ethylene oxide gas were probably absorbed by the powder of the gloves, inducing dermatitis on direct contact with the skin and asthma when the powder was airborne after the patient had turned the gloves inside-out, a mechanism reported in latex allergy."

❖ The Environmental Defense Fund (EDF), a New York-based environmental group with 250,000 members nationwide, is suing seven hospitals in Sacramento, Calif., for failing to notify local residents of EtO emissions as required by Proposition 65. Proposition 65, adopted by California voters in 1986, requires businesses to warn individuals before exposing them to a chemical known to cause cancer or reproductive harm. The EDF is seeking civil fines from the hospitals in the amount of $2,500 per day for each person exposed to EtO without warning. At press time, hearings and negotiations were still underway to determine the outcome of the suits, which were filed in June 1995. Spokespeople from the hospitals maintain that the EtO emissions did not create a community health hazard; however, all have taken steps to reduce or eliminate the use of EtO.

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