Major article

New developments in disinfection and sterilization

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A review of regulatory clearances for selected new sterilization and disinfection products for the period January 2012-June 2015 indicates continued leverage of established technologies for steam and low-temperature sterilization, and high-level disinfection. New products in these areas were typically modified and improved versions of existing products, with the exception of a new combination hydrogen peroxide/ozone sterilizer. Development of new low-temperature sterilization technologies to address continued evolution of complex medical devices is expected to continue.

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Technologies and products used by health care facilities for disinfection or sterilization of medical devices are constantly undergoing evolution and development. However, in the United States, the product choices actually available to health care facilities for use in their reprocessing departments are regulated by the Food and Drug Administration (FDA). Products or equipment used for disinfection or sterilization of medical devices are typically considered Class II medical devices under the US Code of Federal Regulations, and are thus required to undergo regulatory review before entry into the commercial marketplace.

Section 510(k) of the Food, Drug, and Cosmetic Act, which is applicable to most products and equipment used for reprocessing of medical devices, requires the manufacturer to notify the FDA of their intent to market a new or modified device by submitting a Premarket Notification, referred to as a 510(k). In the submission the manufacturer must provide data and information to demonstrate the new or modified device is "at least as safe and effective, that is, substantially equivalent, to a legally marketed device," often referred to as the predicate device. The FDA reviews the information provided in the submission, and may ask the manufacturer for clarifications, or for additional information. If, at the conclusion of the review, FDA is satisfied that the new or modified product meets the requirements for substantial equivalence, FDA will issue an order of substantial equivalence, most often in the form of a letter, clearing the device and allowing the manufacturer to place it in commercial distribution.

A method for evaluating and summarizing recent developments in disinfection and sterilization products and technologies, with emphasis on those that can have immediate application and effect, is review of recently cleared 510(k)s. The list of cleared 510(k)s is updated monthly and can be readily searched on the FDA Web site. Although clearance of a 510(k) does not require the manufacturer to proceed with commercialization, in most cases the research and development investment required to create or modify the product, and the regulatory expenses involved with the preparation and submission of the 510(k), most commonly leads the manufacturer to commercialize the product after clearance. We reviewed selected 510(k) clearances of sterilization and disinfection products since 2012. It was not intended to be a comprehensive review of every related product clearance in that time frame, but rather, it is a selection of clearances that provides an overview of developments in the field. This article provides an update to a recent publication on this topic that also incorporated some of this approach.

Sterilization processes used in health care facilities can be broadly divided into high-temperature processes (eg, saturated steam) and low-temperature processes. The low-temperature processes were developed to allow terminal sterilization of medical devices unable to withstand high temperature (eg, >60°C) and high humidity. Low-temperature sterilization processes use gaseous chemical sterilants (eg, ethylene oxide and hydrogen peroxide) and are based on chemical action (eg, alkylation and oxidation). Disinfectants are categorized as high-level, medium-level, or low-level, depending on their expected application and efficacy.

DEVELOPMENTS: HIGH-TEMPERATURE (STEAM OR MOIST HEAT) STERILIZATION

Sterilization with saturated steam is well characterized and has been used in health care facilities for decades. The equipment and processes have evolved over time, with significant changes made

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to improve ease of use, safety, efficacy, and cycle time. Examples of these changes include increasing the typical steam sterilization process temperature from 121°C to the range of 132°C-135°C, and the increasing use of dynamic air removal techniques such as vacuum-assist and steam-flush-pressure-pulse systems.

A search of the cleared sterilizer 510(k)s from January 2012-June 2015 (See Fig 1) indicates 10 510(k) clearances for steam sterilizers. A review of the available 510(k) summaries indicates that the majority of these clearances were for sterilizers with a different (typically larger) chamber size than the predicate device. Clearances also included sterilizers with modified cycles, and design or software modifications to existing sterilizers.

Device Name | Applicant | 510(k) Number | Decision Date
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Sterrad NX Sterilizer, Sterrad 100 NX Sterilizer Products | Advanced Sterilization Products | K142454 | 04/03/2015
Sterisale Hp Table Top Steam Sterilizer | Milton E Pedrazzi D.d.s inc. | K140736 | 01/20/2015
3M Steri-Vac Sterilizer/Aerator | 3M Company | K142034 | 01/08/2015
Sterizone Sterilizer | TS3 Inc. | K141163 | 12/17/2014
Fort Defiance Automated Steam Sterilizer | Fort Defiance Industries, Inc. | K141009 | 12/16/2014
Sakura Steam Sterilizer A12, A0 | Sakura Seiki Co., Ltd | K132439 | 01/06/2014
Belamed Steam Sterilizer MS1-V | Belamed, Inc. | K130172 | 09/23/2013
Getinge 800hc Series Steam Sterilizer | Getinge Sourcing Lic | K122625 | 05/22/2013
Sakura Steam Sterilizer Model -AH06 | Sakura Seiki Co., Ltd | K122774 | 05/09/2013
Getinge 633nc Steam Sterilizer Air Glide | Getinge Sourcing Lic | K120532 | 05/02/2013
Getinge 400hc-E/ Series Steam Sterilizer | Getinge Sourcing Lic | K122071 | 03/12/2013
Sterrad 100 NX Sterilizer Duo Cycle | Advanced Sterilization Products | K111377 | 09/13/2012
Getinge 700hc-e Series steam sterilizer | Getinge Sourcing Lic | K120441 | 05/31/2012
Skytron Integrity 215 Steam Sterilizer | Sakura Seiki Co., Ltd | K120149 | 05/08/2012

Other clearances in the area of steam sterilization included new or modified biological indicators for monitoring the efficacy of steam sterilization processes (See Fig 2). There were 2 510(k) clearances for biological indicators with reduced (shortened) incubation times. Shorter biological indicator incubation times facilitate faster decision making by the health care facility about the quality of the sterilization process and appropriateness of releasing the processed devices for use on patients.

The SporView 10 Steam Self-Contained Biological Indicator from SPSmedical Supply Corporation (Rush, NY) was cleared under 510(k) file K122024 during November 2013. This self-contained biological indicator is intended for monitoring steam sterilization processes.


Device Name | Applicant | 510(k) Number | Decision Date
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SporView 10 Steam Self-Contained Biological Indicator | SPS Medical Supply Corporation (Rush, NY) | K122024 | 11/26/2013
Sterrad Cyclesure 24 Plus Biological Indicator | Mesa Laboratories | K140589 | 12/03/2014
Sterilucent Self-Contained Biological Indicator | Sterilucent, Inc. | K141238 | 11/03/2014
3M Attest Rapid Readout Biological Ind. | 3M Company | K140392 | 08/13/2014
VERIFY V24 Self-Contained Biological Ind. | Sierra Corporation | K140499 | 07/17/2014
VERIFY V24 Self-Contained Biological Ind. | Sierra Corporation | K140708 | 08/16/2014
Spsmedical SporView 10 Steam SCBI | SPS Medical Supply Corporation (Rush, NY) | K122024 | 11/26/2013
Sterrad Cyclesure 24 Biological Indicators | Advanced Sterilization Products | K123017 | 12/26/2012
3M Attest Super Rapid Readout Biological Ind | 3M Company | K121484 | 10/19/2012
Sterrad Cyclesure 24 Biological Indicator | Advanced Sterilization Products | K122044 | 10/4/2012
Sterifloc Cyclesure 24 Biological Indicator | Advanced Sterilization Products | K111376 | 08/14/2012
NAMSA Steam SCBI | North American Science Assoc. | K113302 | 01/20/2012

The design change included a new optimized growth media formulation that allows a final reading after 10 hours of incubation.\textsuperscript{4,5}

The Attest 1492V Super Rapid Readout Biological Indicator from 3M Company (St. Paul, MN) was cleared under 510(k) K121484 during October 2012. This self-contained biological indicator is also intended for monitoring steam sterilization processes. The new design of this biological indicator included a new sleeve design, optimized media, and a new incubation/reader system that enables a final reading after 1 hour of incubation.\textsuperscript{6,7}

In other steam sterilization developments (not related to FDA clearances), van Doornmalen Gomez Hoyos et al\textsuperscript{8} studied the effects of orientation of a lumened medical device on the physical conditions inside of the lumen during the steam sterilization process. The study included insertion of a thermocouple wire into the lumen of the device (phaco handpiece) to compare temperature measurements inside the lumen, when the device was oriented horizontally and vertically. The study indicated that horizontal orientation did not result in sterilization conditions inside of the lumen, most likely due to steam condensate blocking the lumen. Sterilization conditions were achieved when the phaco handpiece was oriented vertically, which allowed drainage of the condensate during the process.

\textbf{DEVELOPMENTS: LOW-TEMPERATURE STERILIZATION}

Medical devices that cannot withstand steam sterilization are reprocessed using lower temperature processes that rely primarily on chemical, rather than physical, effects to achieve lethality. In health care facilities, ethylene oxide and hydrogen peroxide have been the primary processes used for low-temperature terminal sterilization of medical devices during the past 20 years. The review of recent 510(k) clearances for these types of sterilizers reveals a mix of new products/technologies and modifications of established systems (See Fig 1).

\textbf{Hydrogen peroxide sterilizers}

The Sterrad Sterilizer System (Advanced Sterilization Products, Irvine, CA) is a multiphase sterilization process that uses exposure to hydrogen peroxide vapor and plasma to sterilize heat and moisture sensitive devices. Three different models (Sterrad 100S, Sterrad 100NX, and Sterrad NX) with different chamber sizes and cycles are available to U.S. health care facilities. The 2 recent 510(k) clearances for this system are related to the Sterrad 100NX. The first, K111377, cleared in September 2012, added the DUO cycle to the list of available cycles (Standard, Flex Scope, EXPRESS) on the 100NX. The DUO cycle was cleared for single-channel polyethylene and polytetrafluoroethylene flexible endoscopes with an inside diameter of 1 mm or larger and a length of 875 mm or shorter. It also can be used on accessory devices that are normally connected to a flexible endoscope during use, and also flexible endoscopes without lumens. The second recent clearance, K142454, included updates to the NX and 100NX software related to interface with health care facility electronic equipment and device tracking and documentation systems.\textsuperscript{9,10}

The 510(k) for a new model of the V-PRO Low Temperature Sterilization System (Steris, Inc, Mentor, OH), the V-PRO 60, was cleared in July 2014 (K140498). This sterilizer, like the other sterilizers in the Steris V-PRO line, uses vaporized hydrogen peroxide without a plasma phase. The V-PRO 60 design includes a 60-L chamber, and 3 sterilization cycles. The 28 minute Non-Lumen Cycle is cleared for nonlumened devices, including nonlumened rigid, semirigid, and flexible endoscopes and nonlumened devices with stainless steel or titanium diffusion-restricted spaces such as the hinged portions or forceps or scissors. The 38-minute Flexible Cycle can sterilize 1 flexible endoscope or bronchoscope with a light cord (if light cord is not integral to the endoscope). The lumen specification for the flexible endoscope is a minimum of 1 mm internal diameter and a maximum of 990 mm in length. The third cycle, the 60-minute Lumen Cycle, is cleared for nonlumened devices and instruments with diffusion restricted spaces, and single, dual, or triple channel endoscopes with the following lumen specifications: single or dual lumens with >0.77 mm internal diameter and a maximum of 410 mm length; and triple lumen devices with >1.2 mm internal diameter and a maximum of 410 mm length, or >1.8 mm internal diameter and a maximum of 310 mm length, or >2.8 mm internal diameter with a maximum of 317 mm length. The VPRO-60 uses Steris’ Vaprox HC hydrogen peroxide sterilant at a concentration of 59%.\textsuperscript{12,13}

The 510(k) for the Sterilucent PSD-85 Hydrogen Peroxide Sterilizer (Sterilucent Inc, Minneapolis, MN) was cleared in October 2014 (K140464). This vaporized hydrogen peroxide sterilizer is designed to meet the requirements for military combat support hospitals. Its fold-out, heavy-duty design allows for easy transportation and setup, and the sterilizer can operate on 1650 watts of power. The sterilizer chamber is 85 L, and the 2 cycles, designated as lumen and nonlumen, use a concentration of 85% hydrogen peroxide vapor at 55°C.\textsuperscript{14,15}

The STERIZONE VP4 Sterilizer (TS03, Quebec City, Canada) received 510(k) clearance in December 2014 under file K141163. This sterilizer is cleared with a single cycle that is intended for sterilization of “general instruments, single channel flexible endoscopes, rigid and semi-rigid channeled devices including single channel and double channel rigid endoscopes.” The STERIZONE VP4 sterilizer uses 2 sterilants, ozone and hydrogen peroxide, in a multiphase process. In the first phase of the process, vaporized hydrogen peroxide is injected into the chamber to a specified pressure. The actual amount of hydrogen peroxide injected can vary based on the size and composition of the load. In the next step of the phase ozone from an onboard generator is injected into the chamber and reacts with residual hydrogen peroxide to form hydroxyl radicals. The entire 2-step phase is repeated, followed by a venting process. This sterilizer uses hydrogen peroxide (125–280 Solution, TS03) and requires a source of oxygen for generation of the ozone. The chamber size is 125 L and the process operates at 20°C–26°C.\textsuperscript{16,17}

\textbf{Ethylene oxide sterilizers}

A new ethylene oxide sterilizer, 3M Steri-Vac Ethylene Oxide Sterilizer/Aerator (3M Company) was cleared under 510(k) file K142034 in January 2015. The 2 models available include 5 cu ft (136 L) or 8 cu ft (224 L) chamber sizes. The user can select a cool or a warm cycle (38°C or 55°C, respectively). The sterilizer uses a single dose 100% ethylene oxide cartridge that provides a fixed gas concentration based on chamber size. Aeration occurs under a vacuum in a locked chamber at the end of the sterilization cycle and is completed without opening the chamber door. This ethylene oxide sterilizer can sterilize single- or dual-channeled rigid or flexible endoscopes along with nonlumened medical devices consistent with the medical devices’ validated sterilization parameters, with up to 20 lumens allowed per cycle.\textsuperscript{18,19}

\textbf{Low-temperature sterilization: Other clearances}

There were a number of additional 510(k) clearances for biological indicators intended for use in low-temperature sterilizers, including 3 separate clearances for biological indicators to monitor the ASP Sterrad sterilizers (see Fig 2). The first clearance (K123017) is for the Sterrad CycleSure 24 Biological Indicator, a self-contained biological indicator manufactured by Advanced Sterilization Prod-
The VERIFY V24 Self-Contained Biological Indicator

Applicant

http://www.fda.gov/medicaldevices/deviceregulationandguidance/

Decision Date

Search term: K142399

Microchem Laboratories, Inc.

K113015 01/30/2012

Low-temperature sterilization: Other technologies

Other low temperature technologies exist that are not cleared for use in health care facilities but are used in medical device manufacturing. Radiation processes such as a gamma or electron beam are frequently used in medical device sterilization but are not suited for use in health care facilities because of safety and cost. Other chemical processes such as chlorine dioxide and nitrogen dioxide have developed specific applications in medical device sterilization. One example, the Nxisizer RTS 360 Industrial NO2 Sterilizer (Nxilizer Inc, Baltimore, MD) uses gaseous nitrogen dioxide at process temperatures of 18°C-30°C. The sterilizer has a 360-L chamber and a cycle time of 80-120 minutes. This sterilizer has not been cleared by the FDA for use in health care facilities.

DEVELOPMENTS: DISINFECTANTS

The FDA regulates disinfectants used in the reprocessing of medical devices. The category or required capability of the disinfectant will depend on the application. For medical devices considered to be semicritical under the Spaulding classification (contacting intact mucosal tissue), high-level disinfection is the minimum requirement. High-level disinfection means capable of deactivating all types of microorganisms except large numbers of bacterial spores. The FDA uses “liquid chemical sterilant” in conjunction with “high-level disinfectant,” because the FDA position is that the only difference between the 2 is contact time. The most common active chemicals in the current commercial high-level disinfectants are glutaraldehyde, orthophthalaldehyde, peracetic acid, and a combination of hydrogen peroxide and peracetic acid.

A review of 510(k) clearances for disinfectants during the period January 2012-May 2015 reveals very little activity in this area. (See Fig 3) The single medical device disinfectant clearance during this time period was for Aldahol V High Level Disinfectant (Microchem Corporation, Euless, TX), cleared under K113015 in January 2012. The Aldahol products are based on the combination of glutaraldehyde and isopropanol. The K113015 clearance was for a new 1.8% w/w glutaraldehyde version of the Aldahol disinfectant.

CONCLUSIONS

Although there has been continued development of products and technologies in the field of sterilization and high-level disinfection since 2012, a review of regulatory clearances required for commercial distribution indicates that most developments have related to modifications or enhancements of existing technologies. Clearances for steam sterilizers, hydrogen peroxide sterilizers, ethylene oxide sterilizers, and high-level disinfectants were examples of new or modified products based on existing technologies. There were also clearances for new sterilization monitoring products, specifically biological indicators, based on leveraging and optimizing existing technologies to provide biological monitoring options for all sterilizers, as well as faster test results.

One cleared product that might be best described as evolving from a new technology is the combination hydrogen peroxide/ozone sterilizer from TS03 Inc. Although ozone technology and hydrogen peroxide technology are well known, this is the first medical device sterilizer for health care facilities that combines these technologies into a single system.

Research into development of new sterilization and disinfection technologies, especially low temperature technologies, will continue. The ongoing evolution of medical devices incorporating more complex designs and specialized materials will drive the continued search for better reprocessing technologies. In the short-term, leveraging of existing technologies to optimize current sterilization and disinfection products will continue to support the process of continuous improvement of medical device reprocessing effectiveness and efficiency.

References


