White Paper

Medical Sterilization Applications

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ABSTRACT

This whitepaper describes the different sterilization methods and technologies available in today's medical equipment sterilization market, that are relevant to rapid prototype models. Focus is given to the more common sterilization methods used or available for medical equipment in hospitals and clinics. At the end of this paper, a conclusion and table summarize six common sterilization methods. These methods/products were isolated and ranked based on their sterilization efficacy and applicability to medical instruments and rapid prototype models.

Sterilization means the use of a physical or chemical procedure to destroy all microbial life, including highly resistant bacterial spores. Bacterial spores are the most resistant of all living organisms because of their capability to withstand destructive agents. Although the chemical or physical process used to destroy pathogenic microorganisms including spores is not absolute, when all parameters of the sterilization process have been met, instruments, supplies and equipment are considered sterile.

An object should be sterilized according to its intended use. Critical objects (those that enter sterile tissues, the vascular system or through which blood flows, such as implanted medical devices) require **sterilization** before use.
Items that touch mucous membranes or intact skin, like endoscopes, respiratory therapy equipment and diaphragms require **high-level disinfection**, which will not be discussed in in details this whitepaper.

Sterilization falls into the following three categories:
• High temperature/pressure sterilization
• Chemical sterilization
• Radiation sterilization

1. Common High Temperature Sterilization Methods

1.1. Steam Autoclave

Steam autoclave is the oldest, safest and most cost-effective method of sterilization in the medical equipment industry. The steam reaches 121-148°C (250-300°F) in the pressure chamber at 15 P.S.I. The sterilization period depends on the temperature and size of the load and can range from 10-60 minutes.

Configurable cycles allow the user to customize the sterilization cycle according to item type, such as hard items, wrapped items, liquids in vented containers, waste and glassware.
The fastest steam sterilization method is flash sterilization and it can be accomplished using either gravity-displacement or pre-vacuum cycles. Flash sterilization is generally the high-speed steam sterilization of an unwrapped instrument or device for three to ten minutes in 132°C saturated steam.

This type of sterilization is intended only for use in hospital operating rooms for urgently needed equipment.

In the steam autoclave process, microorganisms are killed by heat; this is accelerated by the addition of moisture. Steam by itself is not sufficient for sterilization. Greater than atmospheric pressure is needed to increase the temperature of the steam to cause the thermal destruction of microbial life.

Application:
Steam autoclave is used mostly for surgical instruments. This method is not well suited for heat sensitive materials; many surgical instruments are not designed to withstand the prolonged heat and moisture of the steam

sterilization process. This leads to alternative sterilization categories: *chemical sterilization and radiation sterilization*, which allow the sterilization of heat and moisture sensitive materials.

2. Common Chemical Sterilization Methods

2.1. Ethylene Oxide (EtO) Gas

Ethylene Oxide gas was introduced in the 1950's. It is an effective, low temperature chemical sterilization method. It takes *longer* than steam sterilization, typically 16-18 hours for a complete cycle. Temperatures reached during sterilization are usually in the 50-60°C range.

Ethylene oxide (EtO) is a chemical agent that kills microorganisms, including spores. EtO gas must have direct contact with the microorganisms on the items to be sterilized. Due to EtO being highly flammable and explosive in air, it must be used in an explosion-proof sterilizing chamber in a controlled environment.

Items sterilized by this process must be packaged with wraps and aerated. The aeration time may be long and it is needed to make sterilized items safe for handling and patient use.

In general, EtO gas is a reliable and safe agent for sterilization when handled properly.

***Application**:*
EtO is used to sterilize items that are heat or moisture sensitive. The disadvantages of EtO gas are that it can leave toxic residues on sterilized items and it possesses several physical and health hazards to personnel and patients that merit special consideration.
Since EtO poses several health hazards, there are two alternative technologies currently available: Sterrad, a plasma phase hydrogen peroxide based sterilizing agent and Steris, a peracetic acid based technology.

2.2. Sterrad - Low Temperature Hydrogen Peroxide Plasma

Low temperature plasma sterilization was introduced to fill the gap between autoclave: high temperature steam sterilization (safest, fastest and least expensive) and EtO gas sterilization, a low temperature method which leaves toxic residues. Low temperature plasma sterilization is a low temperature, non-toxic but fairly expensive sterilization method. In this process, hydrogen peroxide is activated to create a reactive plasma or vapor.
The Sterrad system is a Hydrogen Peroxide Gas Plasma Sterilization system with an operating temperature range of 45-50°C. Operating cycle times range from 45-70 minutes, depending on system size.

This sterilization system uses a combination of hydrogen peroxide and low temperature gas plasma to quickly sterilize most medical instruments and materials without leaving any toxic residues. Sterilization by this method occurs in a low moisture environment.

The Hydrogen Peroxide Plasma Process Using Sterrad:
The process consists of *two* consecutive and equal sterilization phases.

Vacuum / Pre-plasma Stage:

• When low pressure is achieved in the vacuum stage, low temperature air plasma is generated. This helps in removing residual moisture from the chamber. The system is vented to atmospheric pressure at the end of this stage.
Sterilization Stage:

• Pressure in the chamber is reduced and an aqueous solution of **hydrogen peroxide** is injected and **vaporized** in the chamber.

• The hydrogen peroxide diffuses throughout the chamber, surrounds the items to be sterilized and starts the inactivation of the microorganisms.

• After the pressure has been lowered, the application of **radio frequency (RF) energy** creates an electric field causing **the formation of low temperature plasma**.

• Free radicals are generated in the plasma by breaking apart the hydrogen peroxide vapor. Once the activated components react with the organisms and kill them, they lose their high energy and re-combine to form oxygen, water vapor and nontoxic by-products.

• This is half of the total sterilization process. The other half of the cycle is completed by repeating the above sterilization steps.

• At the completion of the second half cycle, the source of RF energy is turned off, the vacuum is released and the chamber is returned to atmospheric pressure by the introduction of filtered air.

Application:
This system is best suited for sterilizing heat sensitive medical equipment such as endoscopic equipment. With two systems, Sterrad provides sterilization solutions for both smaller and larger applications.

2.3. Steris System | Sterile Processing System

The Steris System is another common, low temperature sterile processing system. It uses the Steris 20 Sterilant Concentrate that combines ***peracetic acid***, a chemical biocidal agent, and a proprietary anti-corrosion formulation to kill microorganisms at low temperature. The process occurs at a temperature of 50-56°C.

The Steris 20 Sterilant Concentrate is mixed with sterile water to create the solution that flows into the sterilization chamber. Sterilization time is 12 minutes.

This is followed by repetitive sterile water rinses to complete the process. The entire process is completed in less than 30 minutes for a standard cycle.

Peracetic acid, by itself, is an oxidant and disinfecting agent for liquid immersion.
It maintains its effectiveness when high levels of organic debris are present. It is an acetic acid with an extra oxygen atom that reacts with most cellular components to destroy cells.

Application:
Only immersible instruments can be sterilized with this method and only a few instruments can be sterilized at one time. No packaging is required.

2.4. Cidex OPA Solution – An Alternative to Glutaraldehyde

Cidex® OPA Solution is a High Level Disinfectant (HLD) for use in reprocessing heat sensitive medical devices. The Cidex OPA Solution provides high-level disinfection in 12 minutes at room temperature (20°C) and is particularly active against mycobacteria.

CIDEX OPA Solution has the broad materials compatibility of glutaraldehyde, requires no activation and has minimal odor. The Cidex OPA Solution is replacing Cidex® and Cidex Plus® due to their toxicity concerns.

Application:
This solution is frequently used on surgical cameras (endoscopes). The item to be disinfected must be thoroughly cleaned and dried before immersion. After immersion, the item must be rinsed thoroughly with sterile water prior to use.

3. Common Radiation Sterilization

3.1. Gamma, Beta Sterilization

Irradiation is an effective sterilization method but limited to commercial use only. The product to be sterilized is exposed to radiation for 10 to 20 hours, depending on the strength of the source. The highest temperatures reached in gamma sterilization are usually 30-40°C. Gamma radiation is popular for sterilizing items before shipment and it can be done through the packaging.

The principal sources of ionizing radiation are **beta** particles and **gamma** rays.
Beta particles, free electrons, are transmitted through a high-voltage electron beam from a linear accelerator. These high-energy free electrons penetrate matter before being stopped by collisions with other atoms. This means their usefulness in sterilizing an object is limited by the density and thickness of the object and by the energy of the electrons. These free electrons ionize the atoms they hit, producing secondary electrons that kill microorganisms.

Cobalt 60 is a radioactive isotope capable of being broken down to produce gamma rays. **Gamma rays** are electromagnetic waves that have the ability to **penetrate a much greater distance than beta rays** before losing their energy from collisions. Because they travel at the speed of light, gamma rays must pass through a thickness measuring several feet before making sufficient collisions to lose all of their energy.

Application:
Radiation can change the properties of some materials like plastics and have adverse affects on glues or adhesives.

As you can see, each of the six common methods discussed above have their advantages and disadvantages.

4. Other Sterilization Methods

In this section, additional, less common sterilization methods are described. These methods either exist, are being replaced by new sterilization methods or are still in development.

4.1. Other High Temperature Sterilization Methods

4.1.1. Dry Heat

This process is conducted at 160-170°C for a minimum of two hours. Due to its high temperatures, its applicable use is limited.
Dry heat in the form of hot air is used primarily to sterilize anhydrous oils, petroleum products and bulk powders that steam and ethylene oxide gas cannot penetrate. In the absence of moisture, higher temperatures are required because microorganisms are destroyed through a very slow process of heat absorption by conduction.

4.2. Other Chemical Sterilization

4.2.1. Glutaraldehyde (Cidex Plus and Cidex)

The Cidex Plus Solution is a disinfectant used to disinfect medical instruments.
It is a 3.4% alkaline glutaraldehyde solution which has tuberculocidal and high-level disinfection capabilities. It achieves high-level disinfection in 20 minutes at 25°C and has up to a 28-day reuse life.

• The Cidex Activated Dialdehyde Solution, aglutaraldehyde solution which has tuberculocidal and high-level disinfection capabilities, is used to disinfect medical instruments and endoscopes. This solution can also be used in an automated reprocessor. It achieves high-level disinfection in 45 minutes at 25°C and has up to a 14-day reuse life.

Both have been used as a cold liquid, high-level disinfectant for heat sensitive equipment.
Note: Cidex (glutaraldehyde) products are being withdrawn from the European market due to concerns that it is toxic and harmful to healthcare staff in hospitals. Also, the U.S. market requires glutaraldehyde-free chemical solutions. This led to the formulation of the Cidex OPA solution.

4.2.2. VHP MD Series

The VHP (Vaporized Hydrogen Peroxide) MD Series Sterilization System for Medical Devices is yet another low temperature sterilization system for packaged medical and diagnostic devices. It is different from the Sterrad system in that it uses hydrogen peroxide in a vaporized form only for sterilization while the Sterrad system uses vaporized hydrogen peroxide to initiate the sterilization and then plasma to complete the process.

In the VHP process, hydrogen peroxide vapor is injected into a chamber via a series of pulses. The cycle time is two hours and the operating temperature ranges from 30-40°C.

Note: This system is a large piece of equipment that uses hydrogen peroxide. In comparison, Steris Corporation's other product, the Steris System 1, is a portable tabletop system that uses peracetic acid to sterilize equipment right before use.

4.2.3. Chlorine Dioxide

Chlorine Dioxide is a liquid chemical sterilization process. The best operating temperature range for this process is 25-30°C when using low concentrations of ClO2. This process requires six hours of contact time to achieve sterilization. The presence of organic matter reduces activity. A processor combines a compound of dilute chlorine gas with sodium chlorite to form ClO2 gas. Equipment is then exposed to this gas in a sterilizing chamber.

4.2.4. Ozone

Ozone sterilizes by oxidation, a process that destroys both organic and inorganic matter. It penetrates the membranes of cells causing them to explode. In this process, a generator is used to convert oxygen to ozone. A six to 12 percent concentration of ozone continuously flows through the chamber. Ozone penetration is controlled by vacuum pressure or by adding humidity. After the process is complete, oxygen is allowed to flow through the chamber to purge the ozone. The cycle time may be up to 60 minutes depending on the size of the chamber or the load of items to be sterilized. Due to ozone gas being corrosive, and it being able to damage moisture sensitive equipment or models, there has not been much use for it in the medical industry.

4.3. Other Radiation Sterilization Methods

4.3.1. X-Ray Sterilization

This is a new process, currently in development, that is based on obtaining X-rays through the conversion of electron beams. The X-rays produced have the same penetrating properties as the rays produced by Cobalt-60 but with this process, treatment is faster, more flexible and more environmentally friendly.

X-rays offer excellent product penetration in sterilization, thoroughly treating the surface and interior of a product.

Conclusion

There are many sterilization methods available on the market; it is critical to know the difference between sterilization methods to tailor the correct one to different material types. Many of the emerging sterilization methods are low temperature based. Steam autoclave is the most widely used, inexpensive and effective sterilization method currently available. Also, historically, many hospitals have relied on EtO-based sterilization systems but due to environmental and safety concerns, they have been investigating alternatives. This white paper also included a discussion of two common, low temperature sterilization alternatives to EtO Gas sterilization: Steris System 1 and Sterrad.

The best, most established, low temperature sterilization method that fills the gap between steam sterilization and EtO gas sterilization is the hydrogen peroxide plasma technology developed by Sterrad. Although Sterrad is an expensive sterilization method, it is effective and versatile. Also, despite its longer cycle time, the VHP MD Series System has its benefits and will become a more common sterilization system in the future. Out of the common methods investigated, listed below are the methods relevant for the sterilization of rapid prototype medical equipment models (low temperature processes, i.e. chemical and radiation methods, are preferable):

Table 1. Sterilization Categories

Sterilization Categories		
	Common Methods	**Others**
High Temperature/ Pressure	• Steam Autoclave	• Dry Autoclave
Chemical	• Ethylene Oxide (EtO) • Sterrad® • Steris System 1® • Cidex® OPA Solution	• Glutaraldehyde • VHP® MD Series • Chlorine Dioxide • Ozone
Radiation	• Gamma	• Electron Beam (E-Beam) • X-Ray

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