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APPLICATION NOTE 5068

STERILIZATION METHODS AND THEIR IMPACT ON MEDICAL DEVICES CONTAINING ELECTRONICS

Abstract: Although there is considerable literature about sterilization methods and equipment, there is very little written about the impact of sterilization on electronics. This article compares popular sterilization methods and discusses their suitability for objects containing electronics.

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Introduction

Thanks to advances in semiconductor and packaging technologies, today integrated circuits (ICs) are found in a widening array of equipment, including medical devices. A particular challenge for medical applications is the need to keep the products sterile—free from harmful contaminants such as fungi, bacteria, viruses, and spore forms. Although there is considerable literature about sterilization methods and equipment, there is very little written about the impact of sterilization on electronics. This application note compares popular sterilization methods and discusses their suitability for objects containing electronics.

Physical Methods

There are several physical sterilization methods, the most efficient of which combines heat with humidity and pressure in a device called an autoclave.

Autoclave Steam Sterilization

Heat sterilization of medical instruments is known to have been used in ancient Rome. The presence of moisture significantly speeds up heat penetration (steam sterilization). The autoclave, invented in 1879, combines heat and moisture with elevated pressure.

How It Works¹

The autoclave is a container similar to a pressure cooker. It is filled with the objects to be sterilized and then sealed. Next, high-temperature steam is forced in under high pressure, thereby displacing air. Moist heat destroys microorganisms by the irreversible coagulation and denaturation of enzymes and structural proteins. The time and temperature to accomplish this depend on pressure and the type of microorganisms to be inactivated. After the necessary time has passed, the steam is released and the sterilized objects are removed. The entire cycle can take from 15 to 60 minutes (batch processing).

Issues

Autoclave sterilization is suited for objects that can tolerate humidity, high pressure (1 to 3.5 atmospheres above ambient), and high temperature (+121°C to +148°C). Typical examples are surgical instruments. Semiconductor devices usually can handle up to +125°C. However, exposing embedded batteries to high temperature significantly reduces their lifetime. Memory devices that use floating-gate technology, such as EEPROMs, can be sensitive to high temperatures. Loss of data integrity should not, however, be expected if the data retention is specified as 10 years at +125°C. Otherwise one should occasionally refresh (rewrite) the memory data to restore the full charge on the floating gates. This works for laser-trimmed EEPROMs. Since the type of trim is usually not specified in product data sheets, it may be necessary to contact the vendor for details.

Chemical Methods

There is a large number of chemical methods for sterilization in the medical field. This section discusses some of the popular methods. Chemical methods can be combined with physical methods.

Ethylene Oxide (ETO) Sterilization

Ethylene oxide (ETO) was first reported in 1859, and gained industrial importance in the early 1900s. ETO sterilization for the preservation of spices was patented in 1938. The use of ETO evolved when few alternatives existed for sterilizing heat- and moisture-sensitive medical devices.

How It Works²

The ETO sterilizer is a container that is first filled with the objects to be sterilized. The basic ETO sterilization cycle consists of five stages (evacuation with humidification, gas introduction, exposure, evacuation, and air washes) and takes approximately 2 1/2 hours, excluding aeration time (removal of ETO). Mechanical aeration takes 8 to 12 hours at +50 to +60°C; passive aeration is also possible, but can take 7 days. After the aeration is complete, the sterilized objects are removed (batch processing). ETO chemically reacts with amino acids, proteins, and DNA to prevent microbial reproduction.³

Issues

ETO sterilization is suited for objects that cannot sustain the high temperature and moisture necessary for steam (autoclave) sterilization. Due to its low +30° to +60°C temperature conditions, the ETO sterilization process is well suited for medical devices with embedded electronics. However, the vacuum may not be acceptable for embedded batteries. There is, moreover, a downside to the method: ETO is a highly flammable, petroleum-based gas and a carcinogen.

Chlorine Dioxide (CD) Gas Sterilization

Chlorine dioxide (CD) was discovered in 1811 or 1814 (both years are listed), and it gained widespread commercial use as a bleaching agent in the paper industry. In 1988, the EPA registered chlorine dioxide as a sterilant. This opened the door for applications in the medical field.

How It Works^{4, 5}

The CD sterilizer is a container that is first filled with the objects to be sterilized. The basic CD sterilization cycle consists of five stages (preconditioning with humidification, conditioning, generation and delivery of chlorine dioxide gas, exposure, and aeration) and takes approximately 2 1/2 hours, including aeration time (removal of CD). After the aeration is complete, the sterilized objects are removed (batch processing). Chlorine dioxide (ClO₂) acts as an oxidizing agent and reacts with several cellular constituents, including the cell membrane of microbes. By "stealing" electrons from them (oxidation), CD breaks their molecular bonds, resulting in the death of the organism by the break up of the cell. Since CD alters the proteins involved in the structure of microorganisms, the enzymatic function is broken, causing very rapid bacterial kills. The potency of CD is attributable to the simultaneous, oxidative attack on many proteins, thereby preventing the cells from mutating to a resistant form. Additionally, because of the lower reactivity of chlorine dioxide, its antimicrobial action is retained longer in the presence of organic matter.

Issues

CD sterilization is suited for objects that cannot sustain the high temperature and moisture necessary for steam (autoclave) sterilization. Due to the low temperature of +15° to +40°C, the CD sterilization process is well suited for medical devices with embedded electronics. CD gas is nonflammable at the concentrations used for this method, and it is not carcinogenic. It does not require high concentrations to achieve sporicidal effects.

Hydrogen Peroxide Sterilization

Hydrogen peroxide was first isolated in 1818. It has a long usage history in the pharmaceutical industry and is a popular alternative to ethylene oxide (ETO). Hydrogen peroxide can be used in two ways: a) vaporized hydrogen peroxide sterilization, and b) hydrogen peroxide plasma sterilization.

Vaporized Hydrogen Peroxide (VHP®) Sterilization

How It Works^{6, 7}

The VHP sterilizer is first filled with the objects to be sterilized. The basic VHP sterilization cycle consists of three stages (conditioning including vacuum generation, H₂O₂ injection, and aeration) and takes approximately 1 1/2 hours, including aeration time (removal of H₂O₂). After the aeration is complete, the sterilized objects are removed (batch processing). The exact mechanism of action of HPV remains to be fully understood and probably varies with microorganisms. Nonetheless, H₂O₂ generates oxidative stress by producing reactive oxygen species, such as hydroxyl radicals, that attack multiple molecular targets, including nucleic acids, enzymes, cell wall proteins, and lipids.

Issues

VHP sterilization is suited for objects that cannot sustain the high temperature and moisture necessary for steam (autoclave) sterilization. Due to its low +25° to +50°C temperature operation, the VHP sterilization process is well suited for medical devices with embedded electronics. The vacuum may not, however, be acceptable for embedded batteries. VHP penetration capabilities are less than those of ETO.

Hydrogen Peroxide Plasma Sterilization

How It Works¹

This method combines chemistry with physics. The hydrogen peroxide plasma sterilizer is first filled with the objects to be sterilized. The basic hydrogen peroxide plasma sterilization cycle consists of four stages

(vacuum generation, H₂O₂ injection, diffusion, and plasma discharge) and takes approximately 1 to 3 hours. Aeration is not required. After the cycle is complete, the sterilized objects are removed (batch

processing). Hydrogen peroxide plasma sterilization inactivates microorganisms primarily by the combined use of hydrogen peroxide gas and the generation of free radicals (hydroxyl and hydroperoxyl free radicals) during the plasma phase of the cycle. Hydrogen peroxide plasma sterilization must not be confused with systems that use ultrasound to create a mist and thus, do not involve electric plasma discharge.

Issues

Hydrogen peroxide plasma sterilization is suited for objects that cannot sustain the high temperature and moisture necessary for steam (autoclave) sterilization. The required vacuum is not as deep as with VHP sterilization. Although the low +40° to + 65°C process temperature is appealing, the 13.56MHz RF energy in the range of 200W to 400W during the plasma discharge phase is problematic for embedded electronics. Hydrogen peroxide plasma sterilization should **not** be used for objects containing semiconductors.

Radiation Methods

Gamma Ray Sterilization^{8, 13}

Gamma radiation was discovered in 1900 when studying radiation emitted from radium. Later, other sources were discovered, such as technetium-99m and cobalt-60. The industrial use of gamma radiation began in the 1950s with cobalt-60 as a radiation source. Cobalt-60 does not occur in nature; it is artificially produced in a reactor. The half-life time of cobalt-60 is 5.2714 years.

How It Works⁹

The objects to be sterilized are put on a conveyor, which transports them to the vicinity of a strong gamma radiation source such as cobalt-60. After stopping in the radiation field so the object receives the required dosage, the conveyor moves on and exposes the next object. Instead of the stop-and-go action, the conveyor could move continuously at a speed that ensures the proper dosage (continuous processing). The ionizing radiation causes excitations, ionizations and, where water is present, free radical formation. Free radicals are powerful oxidizing (OH, HO₂) and reducing (H) agents, capable of damaging essential molecules in living cells. Thus, all three processes cause disintegration of essential cell constituents such as enzymes and the DNA. This results in cell death. The most biological damaging forms of gamma radiation occur in the gamma ray window, between 3MeV and 10MeV. Cobalt-60 emits gamma radiation at the 1.17MeV and 1.33MeV level, somewhat below the most effective range.

Issues¹⁰

Gamma radiation penetrates deep into the irradiated objects. It is faster than physical and chemical methods; it takes place at elevated room temperature and at normal atmospheric pressure. The irradiator is a large object with 2m thick concrete walls to shield the environment from the radiation. Due to the radioactive decay, the exposure time needs to be adjusted regularly to maintain a constant radiation dosage. Besides affecting living cells, gamma radiation also affects polymers and semiconductors. The effect on electronics depends on the dose and dosage rate. In the extreme, a total ionization greater than 5000 rads in silicon delivered over seconds to minutes degrades semiconductor materials for long periods. In practice, the medical industry, for example, sterilize instruments and products at ionization levels in the 250 to 500 rads range, where specifically design semiconductor devices can reliably operate. Therefore, under the right conditions, gamma ray sterilization can be used for objects containing compatibly designed semiconductor devices.

Electron Beam Sterilization¹¹

Because they were emitted from the cathode of an electron tube (also known as a vacuum tube), electron beams were originally called cathode rays. The cathode ray tube (CRT), which generates and deflects an electron beam to scan a fluorescent screen, was invented in 1897. It became a household item with the introduction of television. In CRTs used for television, the electrons of the beam are accelerated with an anode voltage of 10kV (black and white) or 25kV (color) and are back in a metallic conductor when they hit the screen. An electron beam generator is similar to a CRT. However, the acceleration voltage can be up to 1000 times higher and the screen is replaced by a window made of titanium foil which lets electrons leave the vacuum, but keeps out gas molecules from the atmosphere. The use of electron beams for sterilization began in 1956 when the medical devices Industry developed the first commercial application.

How It Works^{9, 12}

The objects to be sterilized are put on a conveyor, which transports them slowly past the window where the electron beam leaves the generator. The conveyor speed is chosen to ensure the proper dosage (continuous processing). Reaching the penetration needed for sterilization requires energy levels in the magnitude of 5MeV to 10MeV. Electron beam radiation forms free radicals that react with macromolecules, thus damaging cellular DNA which leads to cell death. This method destroys all types of pathogens including viruses, fungi, bacteria, parasites, spores, and molds.

Issues

Electron beam radiation does not penetrate as deep as gamma radiation. It is, however, faster than gamma ray sterilization, does not generate nuclear waste, and takes place at an elevated room temperature at normal atmospheric pressure. Electron beam radiation has a better compatibility to materials than gamma radiation. When directed at electronic components, the electron beam can cause charge build-up (ESD) which, in turn, can cause damage. Therefore, electron beam sterilization should only be used for objects containing semiconductors that are designed to specifically tolerate both the electron beam radiation level and ESD build-up.

Conclusion

There are physical, chemical, and radiation methods to sterilize objects for medical applications. Each sterilization method has its special characteristics, which may or may not be compatible with semiconductor devices. When choosing a particular method, one should consider the potential side effects, especially when electronics are involved.

Table 1 summarizes the methods discussed in this article and their compatibility to embedded electronics. Chlorine dioxide has no known adverse effects on electronic components and is, therefore, the best overall choice for compatibility with electronic components. Ethylene oxide and vaporized hydrogen peroxide are also excellent sterilization methods for electronic medical devices that do not include batteries. The epoxy packaging material of ICs is not exposed to chemical sterilization agents and, therefore, cannot be affected. If irradiation immunity is required, specially designed and compatible ICs must be used.

Table 1. Sterilization Methods and Their Compatibility

Sterilization Method	Problematic Parameters	Compatibility
Autoclave steam	High temperature, humidity	Can affect floating-gate memory cells (EEPROM); reduces the lifetime of embedded batteries (if any).
Ethylene oxide	Flammability, carcinogen	The vacuum can affect embedded batteries.
Chlorine dioxide	None	There are no adverse effects on electronics or batteries.
Vaporized hydrogen peroxide	Vacuum	The vacuum can affect embedded batteries.
Hydrogen peroxide plasma	Vacuum, plasma discharge	The vacuum can affect embedded batteries; the RF energy required to generate the plasma may not be compatible to semiconductors.
Gamma ray	Radiation, nuclear waste	The radiation can damage semiconductors that are not designed for exposure.
Electron beam	Radiation	The radiation can damage semiconductors that are not designed for exposure.

Disclaimer

The research for this application note was conducted in June of 2010 and relied solely on material available to the general public (see [References](#)). Since then there may have been technological improvements in methods and equipment as well as changes in legislation. All this could affect the correctness of the descriptions and conclusions above. Therefore, before exposing medical devices that contain electronics to any sterilization method, including those that are not mentioned here, contact the medical device vendor to verify whether the medical device will be harmed by the sterilization equipment that you intend on using.

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