FDA Regulated Sterilization Methods

Understanding FDA regulated sterilization techniques, their impact on polymers, and applications in industry.
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Overview

The final stage in the manufacturing process for medical devices and life sciences products is sterilization. When it comes to sterilizing your equipment, you want to be sure that you’re getting the job done right. The FDA regulates four critical forms of sterilization: autoclave, dry heat, ethylene oxide, and irradiation. Irradiation includes both gamma ray and electron beam methods.

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Autoclaves

An autoclave, which is regulated by ISO 17665, can be thought of as a large pressure cooker. It functions by using steam and specific parameters like time, temperature, and pressure to kill microorganisms. Typically, autoclaves operate within a temperature range of 115° C to 134° C. Their cycle time is measured in increments of minutes. The most common standard for autoclaving is a temperature of 121° C and a pressure of 15 psi, maintained for a time period of 8-30 minutes. The number of cycles, cycle time, and pressure will vary depending on material characteristics.

In many cases, items that are sterilized in an autoclave are placed into a secondary container made of polypropylene. This material, which can be sterilized itself using an autoclave, can be subjected to autoclaving for several cycles without experiencing damage. Polypropylene should not, however, be used during a dry heat sterilization process, since its melting point of 160° C is lower than the temperature most commonly used for dry heat sterilization.

Autoclaves are used to sterilize many products in both the medical and pharmaceutical industries. These include medical instruments, gowns and drapes, and glassware. Pipette tips, which are made of high density polyethylene, are commonly sterilized using the autoclave method. High density polyethylene, while durable enough to withstand the autoclave cycle several times, can withstand only a limited number of these cycles before experiencing damage.
Autoclaves are also used in the food industry to sterilize food packaging that is made of polypropylene or unplasticized polyvinyl chloride. This method allows for evaluation of the shelf life of a product in the consumer industry and can be very beneficial when sending products to geographic locations that have higher temperatures and relative humidity compared to where the product itself is manufactured.

**Dry Heat**

Dry heat, which is regulated by ISO 20857, can be thought of as introducing materials that need to be sterilized to a large oven. Temperatures approaching 170° C are most common, but the dry heat range includes 135° C to 170° C. While both autoclaving and dry heat produce similar results, most facilities choose autoclaving over dry heat. The methods, however, are both highly effective.

The biggest concern with dry heat is the melting or softening point of the polymers used on the materials that need to be sterilized. If the melting point or softening point of the polymer is lower than the temperature necessary for sterilization, the material will warp, often rendering the product useless. For this reason, high heat polycarbonates or high temperature thermoplastics are most compatible for use in an autoclave or dry-heat sterilization process.

There are several materials that can not be sterilized using either dry heat or the autoclave method. These include anything with electronic components or batteries, since the high heat and humidity will damage the components.

**Ethylene Oxide (EtO)**

Ethylene oxide, regulated by ISO 11135, is an industrial chemical used for sterilization. There are three different compositions of ethylene oxide gas used in the sterilization process: 100% EtO, 10% EtO, and 8.6% EtO. Currently, ethylene oxide is diluted with hydrochlorofluorocarbons (HCFCs). In 2015, however, an initiative was launched to substitute the use of HCFCs with carbon dioxide (CO2). CO2 yields similar sterilization results, but is more cost effective for the companies using it. By the year 2030, the use of HCFCs for ethylene oxide dilution will be replaced with CO2.

Dilution of ethylene oxide is required for a number of reasons. It is highly flammable, carcinogenic, explosive, and an alkylating agent. As a result, sterilization using ethylene oxide takes longer than other common sterilization methods. The ethylene oxide sterilization process is broken up into three stages.

**Preconditioning**

In the preconditioning stage, the chamber that will contain the EtO gas is prepared. This chamber is set to a high temperature and high humidity (the exact conditions will vary based on the properties of the materials). After a few hours, the temperature in the chamber will be lowered to somewhere in the range...
of 50° C to 60° C. The lower temperature range used in this process makes EtO an excellent sterilization method to use with thermosensitive polymers.

**Sterilization**
Once the chamber has been prepared, sterilization will take place. In this stage, note must be taken of the material properties, the time of exposure to the EtO, and the concentration of the EtO used. EtO concentration should be in the range of 200mg/L to 800mg/L.

**The Degasser Stage**
After sterilization has been completed, the product moves into the degasser stage. During this stage, the toxic EtO gas is allowed to aerate. Once this process is complete, the product will be completely sterile, and the EtO will no longer be a danger. The aeration period is longer for silicone materials, since silicone will hold onto EtO gas longer than other polymers.

Caution should be used when using EtO to sterilize glass or metals. Because these materials are nonporous, EtO can be used to sterilize the surface of the material, but it can’t penetrate to sterilize other parts of the material.

EtO is most beneficial in the sterilization of items that have electronic components, complex designs, or are in packaging. It is commonly used in the food industry for the preservation of spices, which have an extremely long aeration period to prevent any of this toxic gas from remaining on the food. In this case, it may take many hours to many days to be sure that the material has been properly aerated. EtO is also used in the consumer industry to sterilize fabrics and other nonwoven materials.

**Irradiation**
Sterilization through irradiation comes in two common forms: gamma ray and electron beam. Each of these methods has its own specific uses and procedures.

**Gamma Ray Irradiation**
Gamma ray irradiation, which is regulated by ISO 11137, uses rays that originate from either Cobalt 60 or Cesium 137, both of which are radioisotopes. Cobalt 60 is the more common origin. Gamma rays, which are about the size of an atomic nuclei, operate on the nanometer level. Despite their small size, however, these rays are highly powerful. Gamma rays can penetrate up to 50cm in depth, which makes them ideal for both materials that have a high density or for sterilizing large volumes of products.

In order to use gamma ray irradiation, the polymer has to have radio-stable properties. The dosage of irradiation, which is critical to the success of the method, is measured in Megrads or Kilograys, the amount of energy absorbed per unit mass. When sterilizing polymers, the acceptable range is 0.5Mrad-1000Mrad. When sterilizing a product for medical applications, the minimum dosage is 2.5Mrad.

This dosage level is critical for a number of reasons. If a polymer is exposed to too high of a dose, than discoloration and yellowing may occur. In addition, the physical properties of the material are changed. Chain scission, which is when there is an increase in elongation and a decrease in tensile strength, or cross linking, which is when there is an increase in tensile strength and a decrease in elongation, may occur as a result of too-high dosage.

High temperature thermoplastics, thermosets, and fluoropolymers are all compatible with gamma irradiation. The fluoropolymer Polytetrafluoroethylene (PTFE) cannot be treated with gamma ray sterilization due to its molecular structure: with exposure to as small a dose as
4Mrad, the material will decrease to only 2% of its initial tensile strength.

In the medical and pharmaceutical industry, sterilization through gamma ray irradiation is great for devices such as syringes made out of Cyclo Polyolefin Co-polymers, implantable devices, and single use products. In the food industry, doses below 1Mrad can be used. This is beneficial in preventing spoilage of food and growth of micro-organisms such as salmonella. Gamma ray irradiation can also be used to sterilize food packaging like polyolefin and polystyrene films. In the consumer industry, this type of sterilization is used for the treatment of cosmetics.

Electron Beam Irradiation
The final sterilization method is electron beam irradiation (e-beam), which is regulated by ISO 13409. In this method, an electron beam, which is made up of a concentrated beam of electrons, is used to sterilize materials. This concentrated beam works like a conveyor belt. Electron beam irradiation has the capacity to sterilize materials up to 5 cm deep. While this is not as deep as gamma ray irradiation, it can operate at a higher dosage. Electron beam irradiation is the only continuous method of sterilization; all of the other methods must be done in batches. That also makes electron beam irradiation the fastest method of sterilization.

Just as in gamma ray irradiation, the dosage of irradiation the polymer is exposed to is critical. Some polymers, such as elastomers, silicones, and high heat polycarbonates, can be sterilized using e-beam. In the medical and pharmaceutical industries, it can be used for the sterilization of wound care dressings, pre-filled syringes, and

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packaging. In the food industry, it is used to sterilize food to eliminate the need for preservatives. The consumer industry uses this method to crosslink wires to their cable insulators and sterilize pet food.

These four methods are the only FDA-regulated methods of sterilization. Each has its advantages and disadvantages. Autoclave, dry heat, and EtO sterilization require additional steps before the product can be handled. EtO sterilization is the most costly method due to the use of the chemical, the training needed in order to sterilize with it, and the length of the process. Gamma ray irradiation and e-beam radiation are the next most costly methods. While dry heat sterilization and autoclave sterilization are the most cost-effective, with autoclave being the most inexpensive sterilization method, these methods also have limitations that must be taken into consideration. Overall, however, all four methods are highly effective in sterilizing materials and preparing them for use.
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