Life Science Outsourcing

Bringing Medical Innovations to Life

Understanding Sterilization: Safeguarding Against Invisible Threats

Sterilization Methods and Validating Medical Devices for Maximum Patient Safety

Introduction

A growing number of medical device innovations are introduced each year to equip medical professionals with solutions designed to enhance patient health. A critical aspect of these devices is sterilization, which ensures the eradication of pathogens to prevent healthcare-associated infections (HAIs). HAIs are prevalent in about 1 in 31 hospital patients in the United States.[1] Annually, sepsis was indicated in approximately 1.7 million cases, or 6% of hospitalizations, culminating in 270,000 fatalities.[2] Proactive measures, with sterilization at the forefront, are paramount for bolstering patient safety and minimizing the detrimental repercussions of HAIs.

This comprehensive guide offers an in-depth look at sterilization and validation services for medical devices, and includes sections on:

- Four Leading Sterilization Techniques: An Overview
- Picking the Correct Sterilization Method for Your Device
- Validating and Maintaining the Sterilization Process

This guide will aid medical device professionals in understanding various sterilization modalities, selecting the right method for a specific device, and recognizing regulatory considerations in the sterilization process.

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Four Leading Sterilization Techniques: An Overview

The following are descriptions of each leading sterilization technique and how they are deployed:

Ethylene Oxide (EtO)

LSO Technician loading a 3M™ Steri-Vac™ Sterilizer to initiate an ethylene oxide sterilization cycle.

Ethylene Oxide (EtO) sterilization leverages a colorless gas that functions at relatively low temperatures. This approach currently stands out as the predominant sterilization technique for medical devices. Products are enclosed within a secure chamber where they are exposed to EtO gas. EtO inactivates microorganisms through alkylation of their molecular structures and genetic material. EtO has excellent compatibility with an array of materials, ranging from plastics and metals to glass.

Gamma Radiation

This sterilization modality uses ionizing radiation in the form of high-energy photons, inflicting damage to the DNA of microorganisms and inhibiting their reproductive capabilities. Typically, gamma radiation at the irradiator emanates from the radioisotope cobalt-60 . The exposure duration within this irradiator is meticulously timed based on many variables, including the nature of the product undergoing sterilization.

Electron Beam (E-Beam) Radiation

Commonly denoted as ‘e-beam’ within the sterilization sector, this technique relies on high-energy electrons from an accelerator to quickly destroy microorganisms. Products are usually aligned on a conveyor system, which transports them smoothly through two opposing electron beam paths. E-beam sterilization is particularly effective for heat-sensitive and/or moisture-sensitive devices that may be incompatible with other sterilization methodologies. The administered e-beam dose can be precision-calibrated to neutralize microorganisms while minimizing risks of harm to the devices themselves.

Steam (Moist Heat)

Steam sterilization is achieved through use of pressurized steam at elevated temperatures inside an autoclave. It is adept at neutralizing detrimental bacteria, viruses, fungi, and various spores that are present on devices and in pharmaceutical products. Though the use of pressurized steam is centuries-old, the modern autoclave is still widely used in industrial sterilization applications. The steam sterilization process is quick, with typical exposure times of less than one hour.

Technician collecting surgical tools following a steam sterilization cycle.

Sterilization Modality	Mode of Action	Typical Process Time	Typical Temperature Range	Humidity Required?	Differential Pressure Required?	Material Compatibility	Product Penetration
Ethylene Oxide	Gaseous chemical	1 to 14 Days	37° C to 60° C	Yes	Yes	■■■■■	■■■
Gamma	Photons emitted from a radioactive isotope	< 24 Hours	20° C to 60° C	No	No	■■■■	■■■■■
E-beam	Electrons emitted from an accelerator	< 2 Hours	20° C to 60° C	No	No	■■■	■■■■
Steam	Heat through pressurized steam	< 4 Hours	121° C to 134° C	Yes	Yes	■■	■■

Picking the Correct Sterilization Method for your Device

Each sterilization method has unique attributes to make it ideally suited for specific devices based on factors like packaging, materials, composition, and sterility requirements. The choice of sterilization technique depends on the device's ability to withstand high temperatures, moisture, or radiation. Factors such as the sterility assurance level required, potential impact on the product functionality, and shelf life are also crucial considerations. A thorough understanding of each method's characteristics and specific requirements of the device are essential for selecting the most appropriate sterilization technique.

There is a critical balance between sterility assurance, product integrity, and undesired byproducts. Too little sterilizing agent may lead to healthcare-associated infections (HAI); too much sterilizing agent may lead to product failures, packaging failures, and/or excess residues. It's recommended to consult with a sterilization expert before selecting sterilization parameters.

Which sterilization technique is ideal for your device?
Use the following breakdown of each to inform your process.

Ethylene Oxide (EtO)

Ethylene oxide sterilization is particularly effective for devices that are unable to tolerate high heat and radiation. It is widely used for pacemakers, surgical kits, syringes, and catheters. This method is beneficial for sterilizing a broad range of materials including plastics, resins, metals, glass, and multi-layer packaging. As a surface sterilant, EtO is unable to travel past hermetic seals and gas-tight fittings.

Gamma and E-beam Radiation

Irradiation methods are known as "cold processes" and are ideal for heat-sensitive devices. Radiation is commonly employed for single-use medical devices, closed containers, and devices with complex geometries. They work well for items such as implants, pharmaceuticals, and biologically-derived products. As Gamma and E-Beam employ ionizing energy to sterilize, they are not suitable for most electronics. For polymeric materials, cross-linking and oxidation may be a concern. While radiation-sensitive materials can be sterilized this way, sterilization may take more effort to validate.

Steam (Moist Heat)

This method is ideal for devices able to withstand moisture and high temperatures. It works well for surgical instruments, implantable medical devices, pre-filled syringes, and vials. However, it may not be suitable for electronic components, fiberoptics, and biological materials.

Material Compatibility:

	Nylon, Paper, PEEK, PET, PETG, Tyvek	Cardboard, EVA, HDPE, LDPE, PC, Polyester, Aliphatic PU	Foil Pouches	PP, PTFE	Aromatic PU (TPU)
Ethylene Oxide	Compatible	Compatible	Not Compatible	Compatible	Compatible
Gamma	Compatible	Compatible	Compatible	Not Compatible	Not Recommended
E-beam	Compatible	Compatible	Compatible	Not Compatible	Not Recommended
Steam	Compatible	Compatible	Not Compatible	Compatible	Not Compatible

Feasibility Assessments

Sterilization compatibility should be considered throughout the product development process. R&D sterilization cycles are recommended to evaluate how your device and packaging respond to the sterilization process. It is important to investigate whether product bioburden can be killed, the device retains its integrity, the product or packaging is damaged, and/or unwanted chemical byproducts are generated. Thorough R&D testing is essential for avoiding time-consuming and costly delays in the future. A proactive approach determines the suitability and durability of the device post-sterilization, contributing to its overall efficacy and safety.

Validating and Maintaining the Sterilization Process

The objective of a validation is to determine that the sterilization process will consistently achieve sterility, while limiting undesirable effects on the medical device and packaging. Sterility in medical and pharmaceutical products is underscored by strict regulatory mandates. These serve to protect patient safety and uphold product integrity. Sterilization validation is a critical process mandated by regulatory authorities such as the U.S. Food and Drug Administration (FDA) and governed by international standards like those from the International Organization for Standardization (ISO). These regulations confirm that all products labeled as sterile are free from viable microorganisms, a crucial factor in preventing infections.

Biological Indicators (BI)

Biological indicators (BIs) containing known quantities of hard-to-sterilize spores are critical tools for EtO and steam sterilization to assess sterilization efficacy. BIs undergo sterilization with the product. After exposure to the sterilizing agent, the BIs are assessed for any residual spores. The absence of viable spores confirms kill. The use of BIs adheres to the ISO 11138 industry standards. ISO 11138-1:2006 outlines general requirements for BIs, including production, labeling, testing, and performance criteria. It sets foundational guidelines applicable across ISO 11138, with later parts detailing requirements for BIs in specific sterilization processes.

LSO Technician reviewing biological indicator strips.

Common Testing Methods

Overkill Approach

For EtO and steam sterilization, overkill approaches are commonly employed due to their simplicity and conservatism. After exposing BIs to a low dose of sterilizing agent, the absence of growth demonstrates a reduction in the number of viable spores. By doubling that dose for routine sterilization, the sterility assurance level is conservatively set. For example: If a half-cycle exposure of 15 minutes resulted in a 6-log reduction of spores, the respective full-cycle exposure of 30 minutes would be expected to have a 12-log reduction.

Bioburden Approach

Radiation sterilization methods are commonly validated using the bioburden-based approach. The approach focuses on controlling the microbial load on medical devices prior to sterilization to verify the effectiveness of the sterilization process. It involves assessing the initial bioburden levels on device samples and establishing bioburden targets to achieve the desired SAL. This approach can be utilized for devices that are sensitive to sterilizing agents. However, it requires meticulous attention to detail and robust process controls to ensure consistent results.

Sterilization Standards to Consider

Several standards specifically address medical device sterilization by providing guidelines to support sterilization processes safety and efficacy. Some of the key standards include:

- ISO 11135: Outlines requirements and guidance for the validation and routine control of ethylene oxide sterilization processes for medical devices.

- ISO 11137: Focuses on sterilization of healthcare products using radiation and includes guidance on validation and routine control of the process.

- ISO 17665: Specifies requirements for the development, validation, and routine control of a moist heat sterilization process for medical devices.

These standards are crucial for effective sterilization of medical devices, which in turn ensures patient safety and regulatory compliance. Depending on your geographic location and markets you operate in, additional standards may be enforced by local regulatory organizations and authorities. It's important to thoroughly research all applicable standards or consult with an industry professional experienced in the regulatory landscape. Their expertise can provide valuable insights and guidance in following specific requirements relevant to your region and verify that your sterilization processes meet industry standards.

Maintaining the Sterilization Process

After sterilization is validated, the process can only be considered validated so long as it is maintained. The regulatory standards provide requirements and guidelines on how to demonstrate process maintenance. Changes that could affect the validated sterilization process must be assessed. Events that might require requalification include, but are not limited to:

- Unexplained failures in sterilization
- Changes to product
- Changes to packaging
- Modification to the sterilization equipment
- Changes to load density
- Changes that impact the product bioburden

There are many ways to demonstrate maintenance of the sterilization process. Standards may dictate when periodic written assessments are sufficient. However, in many cases, periodic testing of the product and/or sterilization process may be required. A sterilization specialist can guide you through the nuanced requirements and ensure compliance with your regulatory body.

Bibliography

1. HAI and Antibiotic Use Prevalence Survey | HAIC Activities | HAI | CDC. 31 Mar. 2022, https://www.cdc.gov/hai/eip/antibiotic-use.html.

2. Rhee, Chanu, et al. "Incidence and Trends of Sepsis in US Hospitals Using Clinical vs Claims Data, 2009-2014." JAMA, vol. 318, no. 13, Oct. 2017, pp. 1241–49. Silverchair, https://doi.org/10.1001/jama.2017.13836.

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Life Science Outsourcing is a performance-driven Contract Manufacturing Organization. Our unique model leverages in house end-to-end solutions and service offerings, coupled with deep regulatory knowledge. This allows us to provide the agility and flexibility that customers need to accelerate their go to market launches, while streamlining their supply chain and mitigating risk.

Our core services include: assembly, packaging, medical package testing, sterilization, reagent packaging & design, thermoforming, and resorbables.

Need Assistance?

Life Science Outsourcing (LSO) holds both an ISO 11135 and ISO 11765 accreditations as a contract sterilizer, alongside its registration with CDER for Drug Sterilization. As a testament to our expertise, LSO manages a comprehensive suite of sterilization services, including in-house ethylene oxide and steam sterilization, while strategically partnering for gamma and e-beam sterilization. Our team, composed of seasoned professionals in sterilization and validation, boasts a record of hundreds of successful validations. Our sterilization services can be seamlessly integrated with any of our other services, ensuring the quickest possible turnaround time while enhancing resilience and redundancy in your supply chain.

Discover the reasons behind Life Science Outsourcing's ability to gain the trust of over 1,800 clients over a span of 25 years.

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