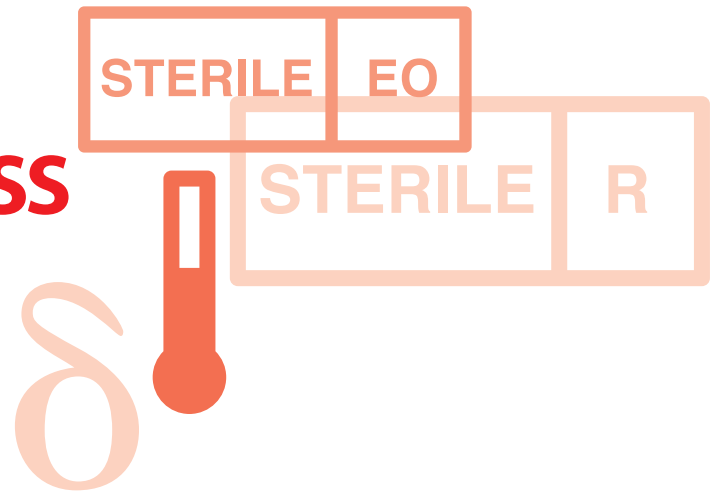


How to Select a Sterilisation Process

A series of guides to tackling manufacturing problem areas.



As the last manufacturing process before shipping, sterilisation issues are often left to the last minute. However, the decision on sterilisation method may have a significant impact on product performance, manufacturing time and cost. As a result, mistakes can be made in haste, which lead to long-term problems. The two major decisions to be made are: which technology to use for sterilisation and whether to outsource this or process in-house. The principal technologies used for sterilising medical devices are ethylene oxide (EtO) 52%, gamma radiation 39%, electron beam (E-beam) 7% and steam 2%. This market-share breakdown has been fairly constant for the last decade except for a slow shift from gamma to E-beam.¹

Ethylene oxide

EtO is cost-effective, provides high levels of sterility assurance and is nondamaging to most materials; processing parameters can be adjusted for heat-sensitive materials. The disadvantages of this method are that it cannot sterilise liquids, airtight containers or certain plastics such as polystyrene. Total processing time typically ranges from two to five

days, includes degassing, which is thus required to remove residuals from the product after sterilisation. Culturing the control spore strips used to confirm sterilisation typically takes seven days. This can usually be reduced to two days by further validation of the process; degassing takes less than two days in all but a few cases. The presence of gas can be demonstrated by heating a sample of the material. There is currently some debate about how much EtO can be released to a patient from a device. Gas handling requires care, but small sterilisers are installed by companies for in-house sterilisation of small, high-value devices such as heart valves, sutures and intraocular lenses. When handled correctly EtO is not an environmental problem, it reacts with water to make antifreeze. Scrubbers can be fitted to large and small sterilisers to render the gas harmless.

EtO sterilisation is suitable for mixed material kits; hollow and suturing needles; most plastics and tubular devices, including, administration sets, cardiovascular catheters, collection bags, drainage catheters, oxygenators and circuits; plasticised PVC; and latex.

Radiation

Gamma sources usually provide more penetrating radiation than E-beam. Gamma sterilisation is cost-effective for large volumes, provides high levels of sterility assurance, is non-damaging to most materials and has fast processing times. It is a continuous process (whereas EtO and steam

are batch processes) and some contractors offer a 24-hour turnaround. The disadvantages of this method include damage to certain plastic materials, the inability to penetrate dense materials and hence an inability to sterilise shadowed areas; heat generated during processing can also cause problems.

High-energy particles are responsible for performing the sterilisation. They do this by disrupting large biological molecules. This disruption can occur in plastics with shortened chain lengths and changes in the amount of cross-linking. This is often expressed as embrittlement of the material or colour modification. Similarly, the absorption of these particles can cause heating in some materials especially metals. Gamma sterilisation uses a bioburden-based kill, which requires excellent clean room control and can restrict the ability to change material suppliers because of the need to audit their bioburden control. It is suitable for commodity products such as dressings, gauze, gloves, instruments, kits, Petrie dishes, scalpels, needles, syringes, and most rigid plastic products especially if opaque. E-beam is similar to gamma although the particles involved are of slightly lower energy and, therefore, are less penetrating. From the perspective of the materials to be sterilised, the pros and cons are the same as for gamma. The capital investment is lower for E-beam and the source can be turned off and is directional, which reduces the need for shielding. Also, there is

What does sterilisation mean?

“For a terminally sterilised medical device to be labelled sterile, the theoretical probability of there being a viable microorganism present on the device shall be equal to or less than 1×10^{-6} .” EN 556 Sterilisation of Medical Devices — Requirements for Terminally Sterilised Devices to be Labelled Sterile.



Table I: Overview of sterilisation validation methods.

Sterilisation method	Basis of validation	Production controls	Release controls
EtO	Biological controls, worst-case challenge and reference load	Bioburden Clean-room sampling Process controls such as humidity, temperature and dwell times.	Culturing of controls, residual gas determination
Radiation	Calibration and dose mapping to give overkill	Bioburden Clean-room sampling, Routine dosimetry	Dose verification
Steam	Biological controls	Bioburden	Culturing of controls

→ some scope for varying the energy level. Because E-beam is not penetrating it can be used to modify the surface of some plastics.

Heat

The most common method of heat sterilisation is the well-proven autoclave. Dry heat may also be used. A microorganism kill is achieved by a combination of heat and time. This method is cost-effective, extremely well documented, simple to use and has fast processing times (autoclave cycles are either 12 min at 134 °C or 20 min at 121 °C).

The disadvantages of this sterilisation method are that the processing temperature exceeds glass transition temperature of all but a few plastics, and it is difficult to organise on a large scale. This method is suitable for metal devices and implants, instruments and nonheat labile fluids.

Alternative methods

A number of other methods of sterilisation exist such as light or ultraviolet radiation or chemicals such as ozone, hydrogen peroxide or more traditional disinfectants. These tend to be used as a production process only when there is a specific reason for using them.

In-house versus outsourcing

Outsourcing sterilisation does not tend to be expensive in countries with a well-established medical device manufacturing base. In these circumstances, it only makes economic sense for the largest companies to build their own facilities. There are some exceptions and small sterilisers are available that employ EtO, which

can be used where it is uneconomic to transport product, or work in progress needs to be minimised, particularly for smaller devices.

Contract sterilisation facilities are often designed for the needs of a few large-volume customers and their operators are often unable or unwilling to meet the needs of small-volume customers with specialist needs. Smaller chambers are available for running nonstandard parameters at some sterilisation contractors.

The limited number of in-house sterilisation units in operation means that good technical support is not readily available in many geographic areas. Because sterilisation is a critical part of the manufacturing process, equipment must be maintained to a high standard. EtO becomes more difficult to operate in-house on a large scale because of gas-handling difficulties.

Gamma radiation is provided by a cobalt source that requires extensive security measures, which are beyond all but the largest companies; as a result few in-house facilities exist. E-beam is the newest of the main technologies and has been enjoying a growth in popularity because of the benefits of fast processing times and lower capital costs. Autoclaves are readily available, but have limited use in medical device production.

Table I gives a brief overview of validation methods to use for each sterilisation process.

Summary

The decision on how to sterilise a medical device is dependant on many factors and as a result requires detailed investigation early in a

project. The key factors are which processes are compatible with the materials and packaging used for the product. Other critical factors are cost, speed, the availability of a technology and level of customer support that is provided.

Reference

1. Medical Device Sterilisation Seminar, Boston, Massachusetts, USA, 14–16 May 2001.

Further reading

- EN1174 Sterilisation of Medical Devices — Estimation of the Population of Microorganisms on Product.
- ISO/AAMI 11134 Sterilisation of Healthcare Products — Requirements for Validation and Routine Control, Industrial Moist-Heat Sterilisation.
- EN 550/ISO/AAMI 11135 Sterilisation of Medical Devices — Validation and Routine Control of Ethylene Oxide Sterilisation.
- ISO 10993, 7, Biological Evaluation of Medical Devices, Part 7 Ethylene Oxide Sterilisation Residuals.
- ISO/AAMI 11134 Sterilisation of Healthcare Products — Requirements for Validation and Routine Control, Radiation sterilisation.
- AAMI TIR 17:1997 Radiation Sterilisation, Material Qualification.
- ISO/AAMI 13409 Sterilisation of Healthcare Products — Radiation Sterilisation, Substantiation of 2.5kGy as Sterilisation Dose for Small Infrequent Batches. [mdt](#)

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