

COMPATIBILITY OF MATERIALS USED FOR STERILE BARRIER SYSTEMS WITH STERILISATION PROCESSES

In selecting materials for sterile barrier systems for medical devices many aspects need to be considered including the following:

- *Microbial barrier properties
- *Compatibility with the device
- *Biocompatibility/toxicological
- *Barrier properties – Moisture, Gases, Light etc.
- *Physical/chemical properties e.g. porosity
- *Method of packing e.g. sealed, folded, taped, need for aseptic opening
- *Material limitations e.g. max. sterilisation T for non-woven materials of polyolefin is 127°C
- *Compatibility with printing and labelling systems
- *Storage limitations
- *Transport conditions
- *Disposal/Recycling requirements

In addition care must be taken to ensure the materials are **compatible with the sterilisation process**. In selecting the materials for sterile barrier systems it is important to understand the sterilisation process that they will be subjected to and its limitations. The sterile barrier system must allow effective sterilisation of the medical device; withstand the process sterilisation process and maintain the microbial barrier after sterilisation. It is essential that any detrimental effects of the process on the materials do not affect the overall functionality of the sterile barrier during subsequent storage and usage of the device.

Sterilisation

Sterilisation refers to any process that effectively renders any surface, equipment or article free from viable microorganisms including spores but not prions (infectious agents based primarily on protein). In practise, it is impossible to prove that all organisms have been destroyed. Therefore **Sterility Assurance levels (SAL)** are used as a measure of the bioburden survival after terminal sterilisation. Expressed as a probability, a SAL of 10^{-6} , for example, means that there is less than or equal to one chance in a million that an item remains contaminated or non-sterile.

Sterilisation techniques

Terminal sterilisation for medical devices can be achieved through a variety of technologies. No single method offers the perfect sterilisation solution for every application. The main ones used in the medical device industry are as follows:

Heat -	Steam, Dry
Radiation –	Electron Beam, Gamma
Gaseous -	Ethylene Oxide, Formaldehyde
Low Temperature Oxidative –	Vaporised Hydrogen Peroxide (VHP), Hydrogen Peroxide/ Gas Plasma

Porous materials are required for all the above processes except radiation and dry heat.

Heat Sterilisation

Moist heat is more effective than dry heat. Death of microbial life by dry heat is a physical oxidation or slow burning process coagulating the protein in cells. In the absence of moisture,

higher temperatures are required than when moisture is present. However, moist heat cannot be used for hydrophilic materials.

High Temperature Steam

Steam sterilisation is typically carried out in an autoclave commonly using steam heated to 121–134 °C. To achieve sterility, a holding time of at least 15 minutes at 121 °C (250 °F) or 3 minutes at 134 °C is required.

Dry heat

Dry heat in the form of hot air is used primarily to sterilise hydrophilic materials or materials that steam and ethylene oxide gas cannot penetrate such as anhydrous oils, petroleum products, and bulk powders. Dry heat sterilisation requires 2 hours holding time at 160 °C.

Although heating provides the most reliable way to rid objects of all transmissible agents, steam and dry heat sterilisation may be overly aggressive for device components or sterile barrier materials and cannot be used for those that are heat or moisture sensitive.

Radiation Sterilisation

Gamma irradiation or E-beam sterilisation are reliable alternatives for low temperature sterilisation but are generally only performed on a contract basis at a limited number of facilities. Ionising radiation produces ions by knocking electrons out of atoms. These electrons are knocked out so violently that they strike an adjacent atom and either attach themselves to it, or dislodge an electron from the second atom. The ionic energy that results becomes converted to thermal and chemical energy. This energy causes the death of microorganisms by disruption of the DNA molecule, thus preventing cellular division and propagation of biologic life. Temperatures generated may still be unsuitable for some materials. The principal sources of ionising radiation are gamma rays and beta particles.

Gamma rays are very penetrating and are commonly used for sterilisation of disposable medical equipment, such as syringes, needles, cannulas and IV sets. Cobalt 60 is a radioactive isotope capable of disintegrating to produce gamma rays, which have the capability of penetrating to a much greater distance than beta rays before losing their energy from collision. Gamma radiation requires bulky shielding for the safety of the operators and storage facilities for the Cobalt-60 which continuously emits gamma rays (it cannot be turned off, and therefore always presents a hazard in the area of the facility). The product is exposed to radiation for 10 to 20 hours, depending on the strength of the source.

Electron beam

Beta particles, free electrons, are transmitted through a high-voltage electron beam from a linear accelerator. These high-energy free electrons will penetrate into matter before being stopped by collisions with other atoms. Thus, their usefulness in sterilising an object is limited by density and thickness of the object. Although less penetrating than gamma rays, electron beams are used as an on-off technology and provide a much higher dosing rate than gamma rays. Due to the higher dose rate, less exposure time is needed and thereby any potential degradation to polymers is reduced.

Irradiation can affect different polymers in different ways. Some effects are detrimental and some are beneficial. The main effects observed are:

- Free radical initiation leading to polymer chain scission or cross linking. (*Scission is the breaking of chemical bonds between atoms in the polymer chain. Cross links are bonds that link one polymer chain to another.*)

- Change in average molecular weight
- Change in physical properties e.g. embrittlement
- Discolouration or gas or odour production
- Oxidation and time dependent effects

Gaseous

Ethylene Oxide

Ethylene oxide (EO or ETO) gas is also commonly used to sterilise objects sensitive to temperatures greater than 60 °C such as plastics or which are moisture sensitive. Ethylene oxide (ETO) is a chemical agent that kills microorganisms, including spores, by interfering with the normal metabolism of protein and reproductive processes, (alkylation) resulting in death of cells. Ethylene oxide treatment is generally carried out between 30 °C and 60 °C with relative humidity above 30% and a gas concentration between 200 and 800 mg/L. It takes longer than steam sterilisation, typically, 16-18 hrs for a complete cycle.

For ethylene oxide sterilisation is essential that materials are porous. Ethylene oxide penetrates well through porous materials such as paper and non-woven materials of polyolefin such as Tyvek® and is highly effective as a sterilant for sterile barrier systems which have adequate porosity. However, ETO gas is highly flammable and toxic/carcinogenic so ETO sterilisation is generally performed on a contract basis. Cycle times are relatively long, particularly post-sterilisation because aeration is required to remove toxic residues.

Formaldehyde

Formaldehyde kills microorganisms by coagulation of protein in cells. Used as a fumigant in gaseous form, formaldehyde sterilisation is complex and less efficacious than other methods of sterilisation. It is used only if steam under pressure will damage the item to be sterilised and ethylene oxide and glutaraldehyde are not available.

Low Temperature Oxidative

Hydrogen peroxide is used to sterilise heat or temperature sensitive articles and materials. It is a strong oxidant and these oxidising properties allow it to destroy a wide range of pathogens. In medical sterilisation hydrogen peroxide is used at concentrations ranging from around 35% up to 90%. The biggest advantage of hydrogen peroxide as a sterilant is the short cycle time. Whereas the cycle time for ethylene oxide (discussed above) may be up to 18 hours, some modern hydrogen peroxide sterilisers have a cycle time as short as 28 minutes.

Vaporised Hydrogen Peroxide (VHP)

This method uses hydrogen peroxide vapour under vacuum to sterilise medical devices. VHP technology demonstrates low toxicity and rapidly decomposes into non-toxic by-products of water vapour and oxygen. Once the vapour has been removed from the sterilisation chamber by a series of vacuum/air pulses, unlike other processes such as ethylene oxide, no further aeration is required.

Hydrogen Peroxide and Gas Plasma

This technology uses a combination of hydrogen peroxide vapour and low temperature gas plasma. After the hydrogen peroxide has sterilised the devices and materials, an electromagnetic field is created in which the hydrogen peroxide breaks apart producing a low temperature cloud that contains ultra violet light and free radicals. Following the reaction the activated components lose their high energy and recombine to form oxygen and water. There is no need for aeration or cool down. Hydrogen peroxide sterilisers have their drawbacks. Since hydrogen peroxide is a strong oxidant, there are material compatibility issues. Cellulose

based materials such as paper products cannot be sterilised using hydrogen peroxide because it reacts with the fibres. This weakens them and also means that there is little if any peroxide left to act as a sterilant. Permeable polymer based materials such as Tyvek® must therefore be used. The penetrating ability of hydrogen peroxide is not as good as ethylene oxide and so there are limitations on what can be effectively sterilised. The vapour is also hazardous with the target organs being the eyes and respiratory system.

Choice of materials

The table below gives some guidelines on material compatibility with the various sterilisation processes but it is important that the medical device manufacturer follows the sterilebarrier manufacturer's recommendations in selecting suitable sterilebarrier systems for their particular products and processes.

Material	Permeability sufficient for steam sterilisation	Permeability sufficient for gaseous sterilisation methods	STEAM (at least one permeable material necessary)	ETO/ Formaldehyde (at least one permeable material must be used)	Hydrogen Peroxide (natural fibre based materials are incompatible)	Gamma/Beta radiation (impermeable materials may be used)	Dry Heat (max temp) (impermeable material may be used)
Medical grade paper	√	√	√	√	x	√	√(160°C)
PET/PP films	none	none	√	√	√	x	x
PET/PE films	none	none	x	√	√	√	x
Non-woven materials of polyolefin	√	√	√ (max T 127°C) not suitable for hospitals	√	√	√	x
PA film (component)	none	none	√	√	√	√	√
PE film (component)	none	none	x	√	√	√	x
PET film (component)	none	none	√	√	√	√	?
Wet laid non-wovens (pulp and plastic fibres)	√	√	√	√	x	√	x
SMS type non-wovens (PP)	√	√	√	√	√	x	x