GUIDANCE DOCUMENT
Compatibility of materials used for Sterile Barrier Systems with sterilisation processes

Sterile Barrier Association

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 temperature for spunbond non-woven materials of polyethylene is 127^0C
- ⇨ Compatibility with printing and labelling systems
- ⇨ Storage conditions
- ⇨ Transport conditions
- ⇨ Environmental aspects e.g. disposal / recycling requirements, consumption of raw material, water and energy during production process, emissions to water, soil and air, etc.

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 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.

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Sterilisation techniques

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

Heat -	Moist Heat (Steam), Dry Heat
Radiation –	Beta respective Electron Beam, Gamma
Gaseous -	Ethylene Oxide, Formaldehyde
Low Temperature Oxidative –	Vaporised Hydrogen Peroxide (VHP), Hydrogen Peroxide Gas Plasma (VH2O2)

Porous materials are always required for the above processes except radiation, dry heat and the steam sterilisation of aqueous liquids.

Heat Sterilisation

Moist heat is more effective than dry heat as it speeds up heat penetration. Although the ultimate cause of microorganism death for both moist and dry heat sterilisation is protein denaturation, it appears that moist heat causes death of microorganisms by a slow burning process coagulating the cell proteins, whereas dry heat is primarily a oxidative process. In the absence of moisture, higher temperatures are required than when moisture is present. However, moist heat cannot be used for hydrophilic materials.

Moist Heat (Steam)

Moist heat 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. Typically used parameters for dry heat sterilisation are 2 hours holding time at 160°C, but other temperatures up to 180°C can be used, for example 1 hour holding time at 170°C or 30 minutes at 180°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 electron-beam (e-beam or beta particle) sterilisation are reliable alternatives for low temperature sterilisation, but are generally only performed at a limited number of facilities due to the higher investment costs involved. Sterilisation services using these methods can be purchased on a contract basis. In these processes ionising radiation damages micro-organisms by breaking chemical bonds and creating reactive free radicals and ions. These species cause further chemical reactions within the cell disrupting its

function. Death of a micro-organism occurs by cumulative damage to the cellular machinery, particularly the DNA molecule, thus preventing cellular division and propagation of biologic life. Temperatures generated may still be unsuitable for some materials with electron beam methods creating the most heat.
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

Gamma rays

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. 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.

Gaseous

Ethylene Oxide

Ethylene oxide gas (EO or ETO) 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.

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For ethylene oxide sterilisation it is essential that materials are porous. Ethylene oxide penetrates well through porous materials such as medical grade paper and polyolefin non-woven materials 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 other sterilisation methods are not available or are deemed unsuitable for the item to be sterilised.

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.

Hydrogen peroxide is a strong oxidant and packaging materials must be chosen to ensure compatibility. 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 non-woven materials of polyolefin 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.

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 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.

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Choice of materials

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

Table 1: Materials with gas and steam permeability

Material	**Permeability** sufficient for steam and gaseous sterilisation methods	**STEAM** at least a part of the packaging needs to be permeable to steam	**EO/FORM** at least a part of the packaging needs to be permeable to gas	**Hydrogen Peroxide** (Plasma) natural fibre based materials are incompatible	**Gamma/E-Beam or Beta radiation** impermeable material may be used	**Dry Heat** (max temp) impermeable material may be used
Medical grade paper	√	√	√	no	√	√ (160°C)
Flush spunbond non-woven materials of polyethylene	√	√ (max. T 127°C) not suitable for hospitals	√	√	√	no
Wet laid non-wovens (pulp and plastic fibres)	√	√	√	no	√	no
SMS (**S**punbond **M**eltblown **S**punbond) non-woven materials of polypropylene	√	√	√	√	no	no

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Table 2: Films and composite films

Material	**STEAM** at least a part of the packaging needs to be permeable to steam	**EO/FORM** at least a part of the packaging needs to be permeable to gas	**Hydrogen Peroxide** (Plasma) natural fibre based materials are incompatible	**Gamma/E-Beam or Beta radiation** impermeable material may be used	**Dry Heat** (max temp) impermeable material may be used
Laminated films, widely used for the manufacture of prefabricated sterile barrier systems (pouches, reels), impermeable					
PET/PP films (PET/Polypropylene)	√	√	√	no	no
PET/PE films (PET/Polyethylene)	no	√	√	√	no
Film components, blister materials, high barrier composites, impermeable					
Aluminium laminates and composites, i.e. high barrier materials	√	√	see suppliers specification	√	√
APET film (Amorphous Polyethylene Terephthlate)	no	√	see suppliers specification	√	no
E/P (Ethylene-Propylene Copolymer)	see suppliers specification	√	see suppliers specification	see suppliers specification	see suppliers specification
HDPE film (High Density Polyethylene)	√ (121°C)	√	see suppliers specification	√	no
LDPE film Low Density Polyethylene	no	√	√	√	no
PA film (component) (Polyamide)	√	√	√	√	√
PE film (component) (Polyethylene)	no	√	√	√	no
PP film (component) (Polypropylene)	√	√	√	no	no
PET film (component) (Polyethylene Teraphthalete)	√	√	√	√	√
PETG (PETG-Foam, PETG-PE) film (PET Glycol)	no	√	see suppliers specification	√	no
PS film (Polystyrene)	no	√	see suppliers specification	√	no
HIPS film (High Impact Polystyrene)	no	√	see suppliers specification	√	no
PC film (Polycarbonate)	√	√	see suppliers specification	√	√
PVC film (Poly Vinyl Chloride)	no	√	see suppliers specification	no	no
TPU film (Thermoplastic Polyurethane)	no	√	see suppliers specification	√	√