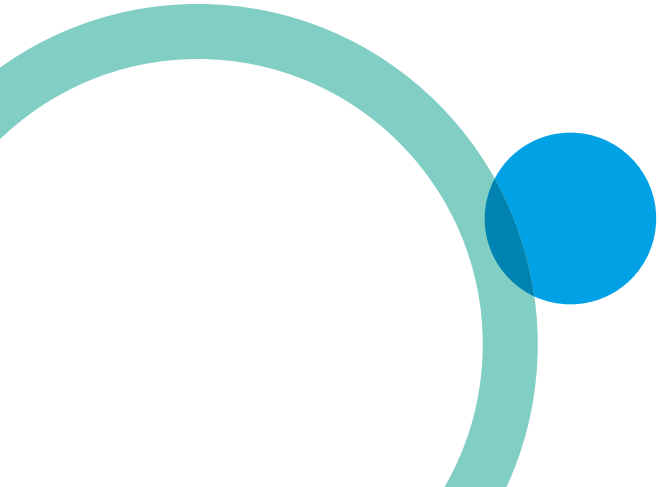
NHS National Services Scotland

Scottish Health Technical Memorandum 01-01

Decontamination of Medical Devices in a Central Decontamination Unit

Part E:

Sterilization by Hydrogen Peroxide or Ethylene Oxide



September 2018

Contents

1. Introduction

1.1 Scottish Health Technical Memorandum (SHTM) 01-01 Part E presents best practice guidance on sterilization by vaporized hydrogen peroxide or Ethylene Oxide (EO) of medical devices in a Central Decontamination Unit (CDU). The chemical structures of these two sterilants are shown, see Figure 1.

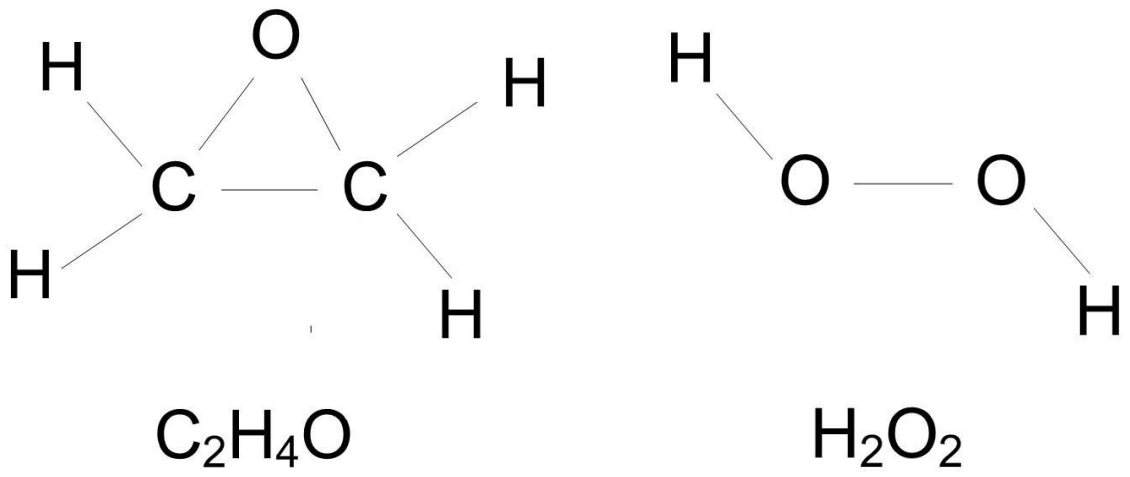


Figure 1: The chemical structures of ethylene oxide and hydrogen peroxide

1.2 Part E is intended as a guide for technical personnel with appropriate training and experience and for Users responsible for the day to day running of hydrogen peroxide sterilizers and/or procurement of sub-contract ethylene oxide sterilization. It will also be of interest to microbiologists, infection control officers, architects, planners, estates managers, supplies officers, and others in both the public and private sectors. SHTM 01-01 Part A describes the decontamination process stages that are required to be undertaken before medical devices are sterilized. Part A also contains a glossary for the SHTM 01-01 series.

Note: GUID 5014: 2016 'Requirements for compliant CDUs' published by HFS requires that the use of porous load sterilizers should be considered first.

1.3 The installation of both the equipment and process needs to work in an environment integrated with other processes within the CDU and surgical facilities. The flow of medical devices being processed should be in line with that of SHPN 13 Part 1: 2011 and that described in section 3 'Decontamination process applicable to the CDU' of SHTM 01-01 Part A: 2018.

Note: The SHPN 13 Part 1: 2011 planning note does not describe on site EO or hydrogen peroxide sterilizers within a Central Decontamination Unit.

1.4 It is possible that no single processes will be suitable for all the medical devices requiring low temperature sterilization in a CDU. In such case a mixed economy of an installed low temperature sterilizer with an alternative sub-contracted process may be required.

Scope

1.5 This guidance covers low temperature sterilization equipment to be used for the processing of medical devices in a Central Decontamination Unit. Two sterilization methods are described i.e. sterilization by vaporized hydrogen peroxide and sterilization by ethylene oxide. It advises on matters to be considered when procuring sub-contract low temperature sterilization (for example sending medical devices for ethylene oxide or hydrogen peroxide off site sterilization) from a Central Decontamination Unit.

1.6 This document, SHTM 01-01 Part E does not provide guidance on the use and operation of ethylene oxide sterilization equipment within NHSScotland CDU facilities. Other sterilization technologies are available and a risk based approach should be used in any assessment exercise.

Precaution

1.7 Loads intended for processing in low temperature sterilizers should not be put into a steam sterilizer as they might not be compatible.

Note 1: For the purposes of this series "**medical device**" is taken to mean as applicable to both a reusable medical device and a single use medical device that is supplied non sterile to the CDU for processing once prior to use. The term medical device as used in the SHTM 01-01 series only applies to those processed through a CDU.

Note 2: Elements of the medical device decontamination process that are applicable to the clinical environment can be found in the SHTM 01-01 supplement guidance GUID 5017. The guidance indicated that surgical instruments were medical devices.

2. Design and procurement considerations

Introduction

2.1 Steam sterilization is well-defined and has been used safely with the majority of medical devices for many years.

2.2 For some medical devices, steam sterilization has a number of limitations particularly in regard to the reprocessing of medical devices that may be damaged by steam at high temperatures or by high pressures. Low temperature sterilization is becoming increasingly required for the reprocessing of thermolabile new technology medical devices. Current low temperature sterilization technologies include ethylene oxide, hydrogen peroxide and ozone. The ethylene oxide standard (See EN11135: 2014 section 3.34) concerning product load volume, defines space within the useable chamber volume occupied by product. The geometric dimensions of the load should also be defined to confirm the load fits within the usable chamber space.

2.3 The medical device manufacturer's instructions for use should be followed in selecting the sterilization method.

2.4 In considering such service improvement, Health Boards and healthcare establishments are advised to consult with their Users on the availability and capability of decontamination services in respect of new medical devices and technologies and the ability to ensure adequate and validated cleaning, disinfection and sterilization.

2.5 Also see SHTM 01-01 Part A on procurement.

2.6 The equipment standard prEN 17180: December 2017 'Sterilizers for medical purposes - Low temperature vaporized hydrogen peroxide sterilizers - Requirements and testing' was published as a draft in December 2017.

2.7 When designing, manufacturing, purchasing and using low temperature sterilization systems, a risk based approach should be used. The designers and manufacturers of systems without a specific process standard will need to have taken account of EN ISO 14971: 2012 'Medical devices: Application of risk management to medical devices'. Health boards and other healthcare organisations using or procuring such sterilizers should also consider the implications of this standard.

2.8 Health Boards should consider the risks to the operator, patient and environment from the use of these technologies while promoting satisfactory clinical service outcomes. Guidance is given in Part A of SHTM 01-01. Users of low temperature processes need to be aware that both periodic testing and product release procedures may be different to those employed for steam sterilization systems.

2.9 Routine monitoring and control systems must be in place to demonstrate each process was delivered within the defined parameters identified during the formal validation process.

2.10 Guidance is given in Part A of SHTM 01-01. Users of low temperature processes need to be aware that both periodic testing and product release procedures may be different to those employed for steam sterilization systems.

2.11 Ensuring effective sterilization is considered to be a key outcome. Validation, defined as achieving an effective, reproducible, sterilization outcome, needs to be conducted to ensure that sterilization has been achieved.

Consideration of low temperature sterilization processes

2.12 The following are characteristics of an ideal low temperature sterilization process (adapted from Schneider, 1994)[1]:

- high efficacy: the sterilizing agent should be virucidal, bactericidal, fungicidal and sporicidal;
- rapid activity with the ability to quickly achieve sterilization;
- strong penetrability and able to penetrate common medical device packaging materials and penetrate into the medical device lumen(s);
- broad material compatibility which produces only negligible changes in the appearance or the function of processed medical devices and packaging materials even after repeated processing;
- nontoxic and presents no health risk to the operator or the patient and poses no hazard to the environment;
- withstands reasonable organic material challenge without loss of efficacy;
- can be monitored easily and accurately with physical, chemical, and/or biological process monitors;
- is cost effective with both reasonable capital costs for installation and revenue costs for routine use.

2.13 The medical device manufacturer's instructions for use should be followed in selecting the sterilization method.

Standard equipment

Sterilizer cycle time

2.14 The time required to complete an operating cycle depends both on the design and configuration of the sterilizer (especially the methods used to remove air from the chamber and to provide sufficient sterilant exposure to the load), the requirements of any aeration stage and on the type and size of load to be processed.

[1] Schneider, P. (1994). Low-temperature sterilization alternatives in the 1990s. TAPPI Journal; (United States), 77:1

Sterilizer chamber size

2.15 The size of a sterilizer is denoted by the volume of the usable chamber space, commonly expressed in litres. The usable chamber space is the space inside the chamber that is not restricted by chamber furniture and that is available to accept the load. It should be distinguished from the total chamber volume, which is equal to the volume of water required to fill the chamber and is therefore larger than the usable chamber space.

Sizing calculation

2.16 For CDUs, the Capacity Planning advice in Scottish Health Planning Note 13 Part 1: 2011 – 'Decontamination Facilities: Central Decontamination Unit' should be used for sterilizer sizing requirements. However, with low temperature sterilization medical device compatibility is normally a bigger consideration than throughput. It is not unusual for departments to require only a single sterilizer of this type. Chamber size in relation to the medical device size may then become the limiting factor.

2.17 Normally where more than one sterilizer of the same type is installed, they should be of the same size and from the same manufacturer. This allows common loading systems to be used, common spare part inventories to be kept, and easier management of maintenance and training. However, in large units medical device compatibility requirements may require low temperature processes from different manufacturers.

2.18 When planning a department or upgrading an existing facility, consideration should be given to ensuring adequate space is available both in the plant room and loading/unloading areas, to account for future replacement and growth of the service and any advancement in technology. Whilst many CDUs may not currently have a requirement for low temperature sterilization, their need in the future should be considered.

Hydrogen peroxide sterilization

2.19 Hydrogen peroxide based sterilization processes are used in a number of CDUs in NHSScotland for processing certain thermolabile medical devices, e.g. medical devices for robotic surgery. They are an established technology and offer a number of features which means that they may be suitable for CDU installation:

- with appropriate independent monitoring systems they can be operated on a parametric release basis;
- the cycle is quicker than many other low temperature processes such as ozone;
- they generally do not need the lengthy aeration times that ethylene oxide or low temperature formaldehyde processes require;
- when operated correctly the by-products are water and oxygen;
- they are now available in a large range of sizes with some units being small enough to be easily moved;
- their installation requirements are relatively simple in that all bar the largest types only need an electrical outlet.

Note: EN 14937: 2009 defines parametric release as a declaration that a product is sterile, based on records demonstrating that the process parameters were delivered within specified tolerances. It also states that parametric release shall only be used if all process parameters are specified, controlled and directly monitored.

2.20 However they also have limitations and these must be considered before their adoption:

- penetration into long lumens may be poorer than with ethylene oxide processes. This will restrict the length/diameter of lumens that can be sterilized;
- there are restrictions in the materials that can be placed in the sterilizer due to interaction of hydrogen peroxide with substances such as cellulose and some precious or anodised metals;
- the methods of sterilant delivery and removal of residual hydrogen peroxide vary tremendously across different manufacturers and therefore medical device compatibility across different models cannot be presumed. Each make and model of sterilizer should have its own medical device compatibility list;
- As at 2017 there is no specific released European standard for these types of sterilizers. A validation, routine control and product release process compliant with EN ISO 14937 should be provided by the manufacturer and agreed with the AE(D) prior to use of the process. The new draft standard prEN 17180: 2017 'Sterilizers for medical purposes - Low temperature vaporized hydrogen peroxide sterilizers - Requirements and testing' should be considered.

2.21 Hydrogen peroxide sterilizers of different manufacturers differ greatly in their approach to vacuum depth, sterilant delivery, sterilant concentration and the methods used for breakdown of residual hydrogen peroxide. For example chamber sizes may vary from 30 Litres to as large as 314 Litres. The geometric dimensions of the load should also be defined to confirm the load fits within the usable chamber space.

2.22 Hydrogen peroxide systems currently on the market within Europe use self-contained, consumable, sterilant delivery methods. These usually take the form of sealed pots or cartridges and are designed to prevent exposure of hydrogen peroxide to the operator when loading and unloading the sterilant. Some may be single shot per cycle types and others may contain enough sterilant for several cycles. The solutions vary in strength from 50% to 59% hydrogen peroxide. Because this strength varies between one sterilizer type and another, they are not interchangeable and hydrogen peroxide must never be decanted from one container to another.

Note: Hydrogen peroxide sterilant solutions are limited to 59% concentration due to the need to satisfy Special Provision A75 of the "Technical Instructions for the Safe Transport of Dangerous Goods by Air" which currently permits sterilization devices containing small quantities of 40 to 60% hydrogen peroxide, UN 2014, to be transported as excepted quantities by passenger and cargo aircraft.

Some sterilizers may have cycles that expose the load to higher concentrations of hydrogen peroxide within the chamber during the cycle. The material compatibility requirements of these cycles may be different to standard cycles.

2.23 There are several methods of residual hydrogen peroxide removal in use:

- gas plasmas generated within the chamber;
- gas plasmas generated external to the chamber (such as in the gas exhaust line);
- the addition of Ozone to the chamber (often called a dual sterilant system);
- catalytic converters.

2.24 The method of residual sterilant removal may impose additional material compatibility restrictions.

2.25 Whichever method is used, the manufacturer must have undertaken an evaluation of residual hydrogen peroxide levels. This would consider the level remaining within the chamber at the end of the cycle, that remaining on the medical device after sterilization and the amount of possible hydrogen peroxide exposure to the operator when unloading the sterilizer. Evidence of this evaluation may be requested as part of any procurement process.

2.26 A medical device that can be sterilized or is compatible with one manufacturer's process may not be compatible with another. There can be no presumption of compatibility with a broad range of sterilizers such as there is with steam sterilization. Refer to the medical device compatibility section for further guidance. Follow the medical device manufacturer's instructions for use.

Hydrogen peroxide sterilizer specification and contract

Introduction

2.27 This section discusses general specifications for low temperature hydrogen peroxide sterilizers and the steps to be taken in inviting tenders and issuing a contract. A specification should be completed as part of the procurement process and submitted as part of a legal contract between the purchaser and the manufacturer. Advice from AE(D)s should be obtained as part of this process. Refer to SHTM 01-01 Part A on procurement of equipment.

Preparing a specification for the hydrogen peroxide sterilizer

2.28 Equipment should be purchased from the NP143 framework for Decontamination equipment, accessories and maintenance. Procurement will need to be undertaken on a bespoke basis with careful evaluation of each supplier.

Standard specifications

2.29 As a minimum, the sterilization process and the sterilizer should be developed, designed, produced and validated in accordance with EN ISO 14937: 2009. Refer to SHTM 01-01 Part A section on procurement of equipment. Note that an equipment standard for hydrogen peroxide sterilizers (EN 17180) was being developed in 2018.

2.30 Compliance with decontamination equipment safety standards is required.

2.31 The sterilizer should be CE marked and manufactured under a quality system complying with EN ISO 13485: 2016.

CE Marking

2.32 Manufacturers should provide certification to the purchaser that the particular design of the equipment is manufactured in conformity with all relevant EU standards. Sterilizers are covered by a number of European Regulations/Directives and are thus required to be in conformance. These include but are not restricted to:

- regulation (EU) 2017/745 on medical devices;
- electromagnetic Compatibility Directive (2014/30/EU);
- low voltage Directive (2014/35/EU), and the;
- machinery Directive (2006/42/EC).

2.33 An evaluation of residual hydrogen peroxide should have been undertaken in accordance with EN ISO 10993-17: 2009 Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances. Also refer to Annex F of prEN17180: 2017.

Water services to the hydrogen peroxide sterilizer

2.34 Larger units with liquid ring vacuum pumps will need connecting to water services. Details of the water-quality requirements, the maximum pressure, minimum pressure and maximum flow rate should be obtained from the sterilizer manufacturer. Flows up to 15 L/minute may be required. Consult with the sterilizer manufacturer to determine their requirements.

2.35 Where multiple units are installed (including a mix of steam and low temperature sterilizers requiring water supplies), there should be adequate capacity to prevent starvation of services as a result of other equipment connected to common supplies.

2.36 Backflow prevention devices should be provided on the water supply as required and need to comply with EN 1717: 2000 and the Water Supply (Water Fittings) (Scotland) Byelaws 2014.

2.37 The temperature of water used for sterilizers with vacuum systems should not exceed the value specified by the manufacturer. Higher water temperatures will reduce the efficiency of vacuum pumps and compromise the specified vacuum levels.

2.38 Performance will also deteriorate if the water is very hard or contains large quantities of solids in suspension. The hardness of the water should be in the range 0.7–2.0 mmol L^{-1}. Hardness values outside these limits may cause scaling and corrosion problems.

2.39 Chlorine and chlorides may cause corrosion of stainless steel in the presence of heat. Advice on maximum permissible levels should be obtained from the sterilizer manufacturer.

2.40 Water economy devices (for example, those that sense the temperature of cooling water and adjust the flow rate accordingly) should be considered in order to reduce water consumption if applicable.

2.41 Further guidance on water supply is given in Scottish Health Technical Memorandum 04-01 – ‘Water safety for healthcare premises’. Refer to Part A: Design, installation and testing.

Drainage

2.42 Larger units with liquid ring vacuum pumps and large chamber volumes will need connecting to drain. Details of the drainage requirements should be obtained from the sterilizer manufacturer.

Electrical supply

2.43 Most units under 60 Litre chamber size can be supplied from a standard 13A socket outlet. Larger units will require connection to a 3 phase supply. Details of the electrical supply requirements should be obtained from the sterilizer manufacturer.

Independent Monitoring Systems (IMS)

2.44 Low temperature, chemical based, sterilization methods have traditionally used biological methods for release of loads. However, many manufacturers of hydrogen peroxide sterilizers now offer an independent monitoring system with the aim of facilitating parametric product release. The cost of such systems can be offset by the reduction in use of biological indicators and faster turnaround of processed medical devices. Parametric release would require to be justified by type testing and verified during validation.

2.45 Regardless of the product release methodology, hydrogen peroxide sterilizers must be purchased with independent monitoring systems that monitor all the key process variables as defined by the manufacturer of the sterilizer.

2.46 The IMS may be used as an aid to parametric release of sterilized product.

Biological indicator systems for hydrogen peroxide sterilizers

2.47 Hydrogen peroxide sterilizers will require the use of Biological Indicators (BIs) as part of any validation and periodic test programme and, where parametric release of product has not been agreed, for product release. These will usually take the form of a self contained indicator which includes the chosen biological challenge (usually 10^6 *Geobacillus stearothermophilus* spores), the growth medium and packaging designed to protect the indicator through the process, keep the spores and growth medium separate until after processing and allow reading of the result without the need to open the challenge device.

2.48 The draft consultation standard prEN 17180 of Dec 2017 on hydrogen peroxide sterilizers stated that biological indicator systems shall comply with EN 11138-1: 2017. Most hydrogen peroxide sterilizer manufacturers will offer their own biological indicator system to use with their sterilizer. A new specific standard on biological indicators for hydrogen peroxide, ISO 11138-6 was being developed in 2018.

Note: Standard EN ISO 14161: 2009 ‘Sterilization of health care products - Biological indicators - Guidance for the selection, use and interpretation of results’ provides general advice on BIs and can be used in the development, validation and routine monitoring of hydrogen peroxide sterilization processes.

2.49 Self contained Biological Indicator (BI) systems will sometimes be of a "rapid readout" type that gives a result based on an accelerated incubation time and reading system. The stated accuracy of such systems may be different than that stated for the full incubation time. If it is intended to use such systems, then the

manufacturer of the incubation equipment should supply information regarding the difference in accuracy between the accelerated readout time and the full incubation period.

2.50 The self-contained BI should be packaged in a manner that is consistent with the medical devices being sterilized.

2.51 The self-contained indicator system should use spores with equivalent resistance as the spores used for validation.

2.52 Self contained biological indicator systems will sometimes include a chemical indicator within (or on) the packaging system to provide rapid indication that hydrogen peroxide has entered the sterilizer chamber.

2.53 When procuring a hydrogen peroxide sterilizer, an evaluation of the recommended biological indicator system should be included with the sterilizer evaluation. This should include the cost of using the indicator system as part any lifecycle analysis.

Chemical indicator systems for hydrogen peroxide sterilizers

2.54 Chemical indicator systems may be recommended by the sterilizer manufacturer as part of a product release and/or independent monitoring system. Chemical Indicators recommended by the sterilizer manufacturer and used by the healthcare organisation should comply with EN ISO 11140 Sterilization of health care products — Chemical indicators Part 1: 2014 General requirements.

2.55 When procuring a hydrogen peroxide sterilizer, an evaluation of the recommended chemical indicator system should be included with the sterilizer evaluation. This should include the cost of using the indicator system as part of any lifecycle analysis.

Packaging systems for hydrogen peroxide sterilization

2.56 Due to the nature of the sterilizing agent used, hydrogen peroxide sterilizers may require specific packaging materials that are constructed of non-cellulose materials. Refer to EN 868 Parts 6 and 7 published in 2017. Also consult Part F of SHTM 01-01.

Ethylene oxide sterilization

Consideration of the use of ethylene oxide for sterilization

2.57 Ethylene Oxide (EO) is a highly reactive liquid and gas which is toxic, flammable and explosive. The safe processing of medical devices within EO sterilizers requires careful consideration of all aspects of the installation and operation of equipment.

2.58 EO sterilizers need to be installed in dedicated areas. EO installations can be expensive both to buy and to run.

2.59 Where there is a clear need for EO sterilization, the service needs be run by a well-supported specialist unit where microbiological testing, environmental controls, degassing procedures and evaluation of residual EO in the sterilized product can be assured.

2.60 EO has its place for sterilization of medical devices especially those which cannot be sterilized by either steam or hydrogen peroxide sterilizers or it is the method specified by the medical device manufacturer.

2.61 Many medical devices that use a combination of heat labile materials and multiple, long lumens over 1000mm may require EO sterilization. To meet this demand there are facilities operated on a commercial scale that can provide sub-contract ethylene oxide sterilization.

2.62 Purchasers of a contract EO sterilization service should be carefully considering the following points:

- validating and monitoring suitable cleaning processes for loads before they are sterilized;
- carrying out representative performance qualification tests for the wide variety of loading conditions that may be used;
- the fact that the efficacy of the process is affected by the packaging used to wrap goods for sterilization;
- since the sterilization process is ultimately dependent upon chemical action, microbiological test methods are required to confirm that sterilization conditions have been attained;
- the difficulty in carrying out meaningful bioburden studies on small numbers of widely differing medical devices to be sterilized;
- the requirement to determine the levels of residual EO and its reaction products when small numbers of widely differing medical devices are processed;
- the need for specialist technical resources dedicated to the operation and maintenance of the equipment.

2.63 The following types of medical devices are suitable for ethylene oxide sterilization:

- wrapped or unwrapped medical devices which would not be sterilized by steam or hydrogen peroxide or would be damaged by doing so. Examples include:
  - heat-labile medical devices with multiple lumens generally over 1000mm (although there are some exceptions to this);
  - some electromedical equipment.

2.64 The following types of medical devices are not suitable for ethylene oxide sterilization:

- medical devices previously sterilized by irradiation;
- medical devices which may absorb and retain unacceptable quantities of EO residuals;
- examples include some ventilatory and respiratory equipment.

Note: There have been many studies undertaken since 1967 warning of ethylene chlorohydrin formation in polyvinyl chloride (PVC) medical devices that were initially sterilized by gamma irradiation and subsequently by ethylene oxide. Some studies confirmed the incompatibility of the sterilization methods whilst others have recently refuted the hypothesis. However until conclusive evidence if provided to the contrary, it is advised not to use ethylene oxide processes on medical devices previously sterilized by irradiation.

2.65 No medical devices should be sterilized by ethylene oxide sterilization unless the manufacturer's instructions for use clearly state that this is an acceptable method.

2.66 EO processes operate at temperatures and pressures which minimise damage to sensitive equipment. Typical operating temperatures are in the range 20-60°C.Two types of EO sterilizer are commonly available for sub-contract use.

Low pressure EO sterilizers

2.67 These are small sterilizers, typically of chamber volumes around 150 litres, where the sterilant is pure EO at sub-atmospheric pressure. The gas is supplied from a single-use, disposable cartridge contained within the chamber. The cartridge limits the amount of EO in use at any one time and reduces the toxic and explosive hazards. The chamber is designed to contain the effects of an explosion of the contents of a single cartridge.

2.68 Low pressure sterilizers are likely to be less expensive to install than larger vacuum sterilizers. The low pressure in the chamber allows pressure-sensitive equipment to be processed though the range of medical devices that can be processed will be less than that of the vacuum sterilizer. This is due to the fact that the vacuum enables more challenging designs of medical devices, such as long narrow lumens, to be processed.

Vacuum EO sterilizers

2.69 These are large sterilizers where the sterilant is EO diluted with another gas.

2.70 The gas mixture is typically chosen to expose the load of packaged medical devices to an EO concentration of around 500-1000 mglitre^{-1} while keeping the potential hazards to a minimum.

2.71 Because of their larger size, vacuum sterilizers require gas disposal plant to remove EO from the chamber exhaust.

EO preconditioning facilities

2.72 For successful sterilization the load should be at a predetermined temperature and humidity before the start of the operating cycle. This may be achieved by exposing the load to the required conditions in an environmentally controlled room or chamber. This preconditioning procedure is considered an integral part of the sterilization process.

EO degassing facilities

2.73 Most, if not all, materials subject to EO sterilization retain varying amounts of EO gas. The residual EO in medical devices must be reduced to a safe level, both for personnel handling the product and for the patient. The general term for this procedure is aeration. Aeration within the operating cycle is known as flushing. Aeration following the operating cycle is known as degassing.

2.74 Other compounds may also be present as reaction products of EO, for example ethylene chlorohydrin and the concentration of these will also need to be reduced. Reference in this SHTM to reduction of EO concentration should be read as applying equally to any other toxic reaction products which may be present.

2.75 Reduction of residual EO occurs naturally as gas diffuses from the product into the surrounding air. Under normal ambient conditions this process may be very slow and significant amounts of EO may be released into the environment. For these reasons degassing by storage under ambient conditions is not recommended. Mechanical degassing should be used.

2.76 A degassing facility may be either a purpose-made aeration cabinet or a room. Some sterilizers incorporate an additional flushing stage as part of the operating cycle.

Design of the load for EO processing

2.77 Packaging materials and methods should be selected which are compatible with the EO sterilization process and which maintain sterility and the quality of the contained product. Packaging should be designed to allow removal of air and penetration of both steam and EO.

2.78 Because a wide variety of EO processes are in use, packaging suitable for one EO sterilizer may not be suitable for another. For example, package seals may be weakened and possibly fail in a cycle with relatively high humidity and several large and rapid changes in pressure, where seals of the same type would have been satisfactory for a cycle employing less extreme conditions.

2.79 The extent to which packaging absorbs or adsorbs EO and its permeability to EO may have a major influence on the efficacy of the cycle and the subsequent aeration process. Cartons (shelf packs, transit cartons) may be convenient but they may increase the humidification time, the gas exposure time and subsequent level of EO residuals.

2.80 Because of the need to control humidity, the extent to which packaging absorbs moisture may have a major influence on the efficacy of the process and must be considered before a satisfactory humidification stage can be demonstrated.

2.81 Process control is also a concern since packaging material that has become dehydrated may absorb excessive moisture during the conditioning phase; if this possibility were not recognised during validation the achieved cycle lethality may be adversely affected.

2.82 In practice, many of the packaging materials routinely used for steam sterilization in hospitals are equally suitable for EO. However, Users should be aware that because

of the lower temperatures employed in the EO process a wider range of materials is available.

2.83 Advice on packaging of medical devices for EO sterilization is given in Part F of SHTM 01-01. Furthermore because of the issues described above, the sub-contract provider should be consulted when selecting the packaging to be used.

2.84 Biological indicators should be placed in the load before preconditioning.

Ethylene Oxide (EO) degassing and residuals

2.85 The residual EO in processed medical devices should be reduced to a safe level, both for personnel handling the medical devices and for the patient.

2.86 Certain materials, such as polyvinyl chloride, silicone and rubber, are particularly absorbent and require longer degassing times. If not removed, residual EO may give rise to burning sensations and other irritant or toxic effects when the sterilized medical device is implanted or in contact with body tissue.

2.87 Reduction of residual EO occurs naturally as gas diffuses from the product into the surrounding air down the concentration gradient. Under normal ambient conditions this process may be very slow and significant amounts of EO may be present in the environment. For these reasons degassing by storage under ambient conditions is not recommended; mechanical degassing should be required of all sub-contract EO sterilization.

2.88 The time required for degassing depends on a number of factors:

- the composition, form and mass of the medical devices in the load;
- the concentration of residual EO when the load is removed from the sterilizer (this will in part depend on the EO concentration and gas exposure time, but more importantly on the extent and nature of the flushing stage in the sterilizer);
- the temperature at which degassing takes place;
- the concentration of residual EO which is acceptable for the intended use of the product.

2.89 Permitted levels of EO residuals, and methods for their determination, are given in EN ISO 10993-7: 2008. When using sub-contract EO sterilization, the provider must have made a determination of residuals in accordance with EN ISO 10993-7 and validated the degassing period.

2.90 The standard EN ISO 10993-7: 2008 specifies limits for EO and Ethylene Chlorohydrin (ECH) residuals in a medical device. No limits are set for Ethylene Glycol (EG) because risk assessment indicates that when EO residuals are within specification, it is unlikely that biologically significant residues of EG would be present.

Matters to consider when selecting an EO sub-contractor

2.91 **Location**

Consider that the proximity of the sub-contract sterilization facility to the healthcare organisation is suitable. One of the major costs associated with sub-contract EO sterilization is associated with the movement of the medical devices to and from the contractor's facility. A facility close to the manufacturer is preferred. Refer to HFS publication 'Requirements for Compliant CDUs', GUID 5014: 2016, for subcontracting. All organisations used for sub-contract EO sterilization should hold EN ISO 13485: 2016 certification for the services being contracted.

2.92 Sterilizer Size

- consider the size of the sterilizer(s) chamber and how much capacity is available;
- determine whether given the chamber size would it be more economical for batches of medical devices to be sent to the sub contactor in one delivery.

2.93 Processing Capability

- consider whether the sub-contractor has the capability to deliver the process with respect to the preconditioning, sterilization, and aeration requirements. Note that the sterilizing time may be a small part of EO process cycle;
- determine whether the facility have enough capacity to deal with your demand. With larger companies this is may not be an issue but if a small scale supplier is chosen, this may result in extended turnaround times as access to chamber space may be limited;
- confirm there is a technical file to demonstrate that the medical devices can be effectively processed.

2.94 Safety

- Determine that the organisation has satisfactory documented records of compliance with safety and environmental regulations. This is important in assuring that the sub-contractor can be relied upon to provide ongoing services.

2.95 Regulatory/Compliance

- verify that the sub contractor holds the necessary medical device quality management system (EN 13485: 2016) certification;
- verify that the services that they are going to provide are within the scope of their certification;
- consider auditing the organisation if sufficient expertise is available or requesting to see audit records from 3rd party audits, internal audits and Notified Body audits. The audits should consider the following:
  - maintenance and calibration programs;
  - validation programs;
  - personnel training;
  - management education and experience;
  - change control and documentation procedures;
  - use of quality systems;

- software validation;
- Health and Safety compliance.

2.96 **Logistics**

- determine how the medical devices will be transported to and from the sub-contractor. Ensure the cost of this is addressed within the contract;
- it should be made clear who provides suitable transport containers;
- verify insurance is in place to cover loss or damage to the medical devices during their transportation.

Sub-contract EO sterilization agreements

2.97 A written agreement between the CDU and the sub-contractor should consider:

- there should be a signed, written agreement/contract that outlines the services and procedures to be supplied and followed by both parties;
- the written agreement should, directly or by reference to existing documents, indicate the responsibilities of each party for ensuring the completion of all quality documentation and process requirements related to the sterilization process;
- the agreement should contain the following:
  - the persons responsible both for the healthcare organisation and the sub-contractor responsible for ensuring quality, for coordinating the flow of information between the parties, and for approving procedural changes;
  - the sub contractor should operate a quality management system in compliance with standard EN 13485: 2016 and maintain their sterilizers through periodic testing as standard EN 1422: 2014;
  - the required documentation (e.g., procedures and processing records) to be used and maintained;
  - details of the medical devices to be processed;
  - the requirements for cleaning of the medical devices before sending to the sub-contractor;
  - the loading configuration including any pallets, chamber loading patterns and wrapping materials and who is responsible for providing the sterile barrier system and packaging the medical devices;
  - if required, the process parameters to be validated by the sub-contractor and the criteria for revalidation;
  - the responsibility and instructions for the placement, retrieval, handling, processing, and maximum time intervals before shipment of Biological Indicators (BIs) and Process Challenge Devices (PCDs);
  - procedures and responsibility for approving sterilization batch records prior to release including quarantine of the medical devices before release for return to the healthcare organisation;
  - content of the batch records to be supplied to the healthcare organisation;

- methods of packaging the sterilized medical devices for return to the healthcare organisation;
- procedures to be adopted should there be a failure in the process leading to non-conforming product. The effects of re-sterilization, if applicable, on product or packaging degradation and EO residuals should be known and a specific provision should be made for these effects. See HFS publication 'Requirements for Compliance CDUs' GUID 5014: 2016;
- third party audit requirements.

2.98 The following is a list of documentation that, at minimum, should be included or referenced in the agreed validation report that will be generated on the agreement of, or when a new medical device is included within, the contract:

- a) sterilization process:
  - preconditioning (if used);
  - performance qualification information;
  - calibration or verification information (or both) for equipment used to monitor or control the sterilization process.
- b) documents:
  - validation protocol, written procedures, or both;
  - final validation report or test summary.
- c) medical device and BI or PCD information:
  - list of medical devices or product families included in the validation;
  - loading configurations;
  - lots and quantity of products used in the validation;
  - rationale for development of product families (if used);
  - rationale for selection of PCD (if used);
  - rationale for selection of most-difficult-to-sterilize location within the medical device;
  - BI label information (manufacturer, lot number, expiration date, spore population, and D-value).

3. Validation

Hydrogen peroxide sterilization validation

3.1 Sterilization is a process whose efficacy cannot be verified retrospectively by inspection or testing of the product. For this reason hydrogen peroxide sterilization processes should be validated before use, the performance of the process should be monitored routinely, and the sterilization equipment should be maintained in accordance with the manufacturer's prescribed schedule. This section provides advice on validation of hydrogen peroxide sterilizers.

3.2 Tests and checks should be carried out to ensure that sterilizers are fit for purpose during the various stages of manufacture, after delivery, during validation and periodically thereafter. Sterilizers should also be tested using a predetermined protocol before being returned to service after modification.

3.3 Advice should be sought from an AE(D) with respect to the status of the test procedures within the SHTM and any changes required by new European Standards.

3.4 The performance of a sterilizer is tested at different times using different procedures. Manufacturers will have devised their own validation regimes based upon compliance with EN ISO 14937: 2009. While this standard is not specific in terms of the type and number of validation tests to be performed, it does require those claiming compliance to have a defined process (called process definition in EN ISO 14937 terms) which demonstrates that sterilizer meets its specified requirements for safety, quality, and performance. These should include type tests and checks performed by the manufacturer. The responsibility for performing type and works tests will normally rest with the manufacturer. The development of a new specific equipment standard on requirements and testing of hydrogen peroxide sterilizers EN 17180 was underway in 2018. Once published this would replace the relevant parts of EN ISO 14937.

3.5 The standard EN ISO 14937: 2009 requires Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ) as with other sterilization processes. The responsibility for testing once installed on-site is dependent upon contractual agreements and/or purchaser preferences and should be performed by qualified personnel. Due to the complex nature of these types of sterilizer, this will normally be the manufacturer or their representative.

3.6 Regardless of who undertakes it, the validation process should be carried out in agreement with the Users, manufacturers and Authorising Engineer (Decontamination) (AE(D)) and be supported by an audit trail. Refer to SHTM-01-01 Part A concerning roles and responsibilities. Consultation with Health Facilities Scotland Decontamination Services is recommended when reviewing new systems and technology.

3.7 The purpose of the validation is to demonstrate that the sterilization process is effective and reproducible. A periodic schedule of validation should be determined and agreed between manufacturer, User and AE(D) based upon a number of factors to include historical data, effectiveness of process repeatability and conformance with established specifications for process parameters

3.8 Since the sterilization process for hydrogen peroxide and ethylene oxide is ultimately dependent upon chemical action, microbiological test methods are required to confirm that sterilization conditions have been attained; the exception being, where a validated parametric release system is in place.

Routine monitoring and control systems must be in place to demonstrate each process was delivered within the defined parameters identified during the formal validation process.

3.9 Guidance is given in Part A of SHTM 01-01. Users of low temperature processes need to be aware that both periodic testing and product release procedures may be different to those employed for steam sterilization systems.

3.10 Ensuring effective sterilization is considered to be a key outcome. Validation, defined as achieving an effective, reproducible, sterilization outcome, needs to be conducted to ensure that sterilization has been achieved.

3.11 As of 2018 there was a published standard for validation and routine control of an ethylene oxide sterilization process for medical devices i.e. EN ISO 1135: 2014. However there was no specific published standard for vaporized hydrogen peroxide sterilizers or their associated sterilization process. A generic standard EN 14937: 2009 could be used for validation and routine control of vaporized hydrogen peroxide sterilization process. Refer to the note for development work in relation to new specific standards being developed for both the vaporized hydrogen peroxide sterilizer equipment and validation of the process.

Note: For process requirements the development of a standard was underway in 2018. The standard reference was ISO/NP 22441 and titled 'Sterilization of health care products -- Low temperature vaporized hydrogen peroxide -- Requirements for the development, validation and routine control of a sterilization process for medical devices'.

Note: The Standard EN ISO 14937: 2009 specifies general requirements for the characterization of a sterilizing agent and for the development, validation and routine monitoring and control of a sterilization process for medical devices. It applies to sterilization processes in which microorganisms are inactivated by physical and/or chemical means. This standard specifies the elements of a Quality Management System which are necessary to assure the appropriate characterization of the sterilizing agent, development, validation and routine monitoring and control of a sterilization process. However it does not describe detailed procedures for assessing microbial inactivation.

Pre-installation checks

3.12 The following checks should be made:

- all the operational, maintenance and validation protocols should be established prior to installation;
- the processes and equipment selected are compatible with the medical devices to be processed;
- the proposed installation location is suitable with regards to available space, ventilation and engineering services;

- preventative maintenance schedules are clearly identified by the manufacturer;
- types of biological and chemical indicators to be used by the healthcare organisation and the equipment supplier are agreed, ensuring the systems offered are compatible with the process and compliant with the relevant international standards;
- contracts are in place for ongoing maintenance and validation;
- daily and weekly housekeeping tasks/tests have been reviewed and agreed to enable them to be included in the department's quality management system and work instructions;
- the manufacturer has supplied the information on the chemicals to be used. This should include safe handling, storage and disposal of any out of date or unused chemicals;
- material Safety Data Sheet (MSDS) have been provided;
- control of Substances Hazardous to Health (COSHH) assessments have been undertaken for both the use and safe storage of the process chemicals;
- appropriate sterile barrier systems and packaging to be used with the sterilization process has been ordered.

Installation Qualification (IQ)

Installation checks

3.13 The majority of hydrogen peroxide sterilizers will not require any ancillary equipment. However for those larger machines that do, when the checks on ancillary equipment require a sterilizer to be in operation, the CP(D) should carry them out in cooperation with the contractor for the sterilizer.

3.14 The contractor for the sterilization equipment is not responsible for the correct functioning of services and ancillary equipment unless this was agreed in the purchase contract.

3.15 Where factory acceptance testing is required, a protocol should be agreed in advance with the AE(D) and included in the procurement contract.

Engineering services

3.16 Checks should be made on the following:

- that the engineering services are installed correctly, are adequate to meet the demands of the equipment, do not leak, and all necessary isolating valves or switches and test points have been installed and are working correctly;
- that drains (if fitted) remove effluent effectively when all plant in the vicinity, including the decontamination equipment, is connected and operating under full demand;
- that the water economy system (if fitted) operates correctly.

Note: Installation tests should determine and provide documented evidence that the equipment is installed and configured to operate in a safe manner and is manufactured, installed and operates in accordance with IEC 61010-2-040: 2015.

The installation qualification testing is a process of obtaining and documenting evidence that the equipment and ancillaries have been provided and installed in accordance with the specification supplied to the manufacturer.

3.17 Electrical equipment on the sterilization equipment should be checked to ensure it is correctly connected to the electrical service in accordance with BS 7671 (IET Wiring Regulations). The following electrical tests should be carried out and certified:

- insulation resistance;
- phase sequence (for three-phase installations);
- polarity;
- bonding and earth continuity;
- emergency stop.

3.18 After the sterilization equipment has been installed, it should be checked to ensure that the following recommendations are met:

- the manufacturer has supplied all the documents specified in the contract;
- the equipment has been supplied and installed in accordance with the contract;
- calibration verification certificates traceable to UKAS certification for the measuring instruments and controller(s) on the equipment have been supplied;
- no defects are apparent from a visual inspection of the equipment;
- all supports, bases and fixings are secure and without imposed strain from service connections;
- thermal insulation is in good condition and securely attached;
- security and settings of door safety switches are in compliance with data supplied by the manufacturer;
- keys, codes or tools required to operate locked controls and control over-rides have been supplied, operate correctly and only operate the control for which they are intended; and cannot unlock controls on other machines in the vicinity;
- loading conveyors and trolleys, load carriers and load baskets are effective and safe in use;
- IT connections are made and connected for the sterilizer system and monitoring instrumentation onto the main server and available for back-up;
- automatic loading equipment should have safety systems verified.

Functional checks during the IQ

3.19 During an operating cycle, with an empty chamber, checks should be made that the following recommendations are met (several cycles may be necessary to complete all the checks):

- the selection of automatic or manual control is by key code or tool;
- the selection of one control mode inactivates the other control mode;
- sterilant, water, steam or compressed air cannot be admitted into the chamber when the equipment is under automatic control until the door is closed, locked and sealed;
- the operating cycle cannot start until the door is closed, locked and sealed;
- if the cycle may be advanced sequentially under manual control – this function should be protected by password/code entry;
- the indicated and recorded values of cycle variables are within the limits specified by the manufacturer throughout the cycle;
- there are no leaks of water, steam aerosols, air, gas or effluent throughout the cycle;
- there is no evidence of interference to or from other equipment connected to the same services;
- operation and reading of all instruments appears to be satisfactory;
- the temperature of surfaces routinely handled by the operator does not exceed 55ºC.

3.20 At the end of the cycle, checks should be made that the following recommendations are met:

- the door opening system cannot be operated until the cycle has been completed;
- for systems incorporating one or more cycle stages at pressures 200 mbar above or below atmospheric pressure:
  - the door opening system cannot be operated until the chamber has been vented to atmosphere and the chamber pressure is within 200 mbar of atmospheric pressure;
  - the door retainers cannot be released until the seal between the door and chamber has been broken, and the chamber is effectively vented to atmospheric pressure.
- each door interlock system is fail-safe;
- failure of one interlock, or any one service, does not allow the door to be opened when conditions within the chamber would cause a hazard, for example pressure in excess of 200 mbar;
- the automatic controller has operated in accordance with the specification.

Response to external faults

3.21 The sterilizer should be checked to ensure it reacts correctly and safely, that is, it does not create a safety hazard or give a false indication of the satisfactory completion of a cycle, when exposed to a number of external fault conditions.

3.22 During each stage of an operating cycle, the response of the sterilizer to the following simulated faults (as appropriate to the type of machine) should be checked, ensuring that the cycle will fail in the event of each fault:

- operation of the emergency stop button;
- power failure;
- compressed air (if fitted) pressure too low;
- compressed air (if fitted) pressure too high;
- water service (if fitted) failure;
- communication failure.

Schedule of validation tests (OQ and PQ)

3.23 The contractor/manufacturer should carry out installation checks and tests before operational tests are performed; these may be witnessed or repeated by the Competent Person (Decontamination) (CP(D)) if required.

3.24 Operational Qualification (OQ) tests and Performance Qualification (PQ) tests should be carried out by the CP(D).

3.25 Where the loads processed by the CDU are likely to present a greater challenge to the sterilization process than those used for operational qualification, performance qualification will be required. The range of OQ tests performed and recommended by the manufacturer should be based on the worst case challenge of medical devices within the compatibility claims of the sterilizer (refer to the section on medical device compatibility). However there may be instances with new medical device designs where this is not the case. If there is any doubt then the advice of the sterilizer manufacture and the AE(D) should be sought before processing such medical devices.

Note: Some manufacturers of hydrogen peroxide sterilizers term a half cycle validation test based upon a PCD containing a biological indicator as a performance qualification test. This is not a PQ tests as commonly accepted as it does not reflect the challenge of an actual production load but is similar in concept to using standard test pack with a steam sterilizer. It has however been deemed a worst case challenge by the sterilizer manufacturer.

3.26 PQ tests should be carried out after the IQ and OQ tests have been satisfactorily completed. PQ tests may be performed while the sensors used in the IQ and OQ tests are still in place and before the final vacuum leak test.

3.27 Schedules for validation tests for a hydrogen peroxide sterilizers are shown, see Table 1. However it should be noted that these are the minimum tests required and that the testing should include all tests required to demonstrate compliance with EN ISO 14937: 2009 as recommended by the manufacturer.

Validation Tests	IQ	OQ	PQ
Installation and safety checks.	X		
Chamber integrity tests as defined by the manufacturer		X	
Automatic control test for each cycle type (no load).		X	
Verification of calibration of both control and IMS instruments.		X	
Half cycle microbiological test with biological and chemical indicators within a process challenge device repeated 3 times for each cycle type fitted.		X	
Any additional tests to meet the manufacturers EN ISO 14937 regime.		X	
Production load test based upon half cycle test and biological indicators.			X

Table 1: Validation tests over the three qualification stages for a hydrogen peroxide sterilizer

Performance Qualification (PQ) tests

3.28 The Performance Qualification (PQ) is the process of obtaining and documenting evidence that the sterilizer will consistently produce reproducible results when operated in accordance with the pre-defined acceptance criteria within the process specification. All PQ tests for hydrogen peroxide sterilizers will be microbiological based and use either biological indicators if a challenge device can be used or directly inoculated production medical devices. Advice from the manufacturer should be sought as to an appropriate way of undertaking these tests.

3.29 The extent of the PQ required will depend on the type of sterilizer and the nature of the load.

3.30 Users should adopt the following procedure for every sterilizer:

- establish a list of potential product families and their relationship to the validation loads;
- establish a list of the different loading conditions to be processed in the sterilizer. Each production load should correspond to one of the listed loading conditions;
- seek advice from the sterilizer manufacturer as to whether each loading condition presents a greater or lesser challenge to the process than the challenge device load used in tests carried out during validation;
- where the loading condition is a lesser challenge than the validation loads, the results of the validation tests may be used as PQ data;
- where the loading condition is a greater challenge than the validation loads, PQ tests should be carried out.

3.31 Where PQ tests have not been undertaken and no PQ report will be created, the AE(D) should satisfy himself/herself that the range of installation, operational and periodic tests undertaken is representative of the range of loads and product families processed by that particular sterilizer. This should be documented.

3.32 The User should decide which loading conditions require PQ tests for all sterilizers following advice from the AE(D) and the hydrogen peroxide sterilizer manufacturer.

3.33 PQ tests should be performed as part of the initial validation procedure, as part of any repeat validation procedure, and whenever the User judges that a new loading condition calls for a new PQ test.

3.34 Where a new load is not covered by an existing PQ report, full PQ tests should be conducted.

3.35 When designing a new loading condition, it is important that the correct packaging is specified with the load. The packaging specification and materials should be to the appropriate standards and not altered without repeating the PQ procedure unless the loading condition with new packaging can be demonstrated to be covered by an existing PQ report.

3.36 Guidance on performance qualification testing of the packaging system is given in SHTM 01-01 Part F.

Half cycle microbiological test

3.37 This approach to low temperature sterilization validation has been widely employed, particularly for medical devices to be processed in healthcare organisations. It is an approach different from that adopted with virgin product. This is because the challenge to the sterilization process is often unknown and variable.

3.38 Therefore, healthcare sterilization processes employ a treatment that exceeds that needed to achieve the specified requirements for sterility. This approach is referred to as the "overkill approach." Guidance on this approach can be found in EN ISO 14161: 2009.

3.39 In short the process can be described as:

- determine the position(s) within the medical devices where it is most difficult to achieve sterilizing conditions;
- create a challenge to the sterilization process, comprising a known number of microorganisms (10^6) with known resistance to the sterilant, using one of the following approaches:
  - placing biological indicators within medical devices at position(s) where sterility is most difficult to achieve;
  - inoculating with reference microorganisms the position(s) within medical devices where sterility is most difficult to achieve.
- Package the challenge in the same manner as medical devices are to be produced routinely;
- Process this challenge under conditions designed to deliver less sterilant than the anticipated production cycle;
- Identify the extent of treatment that inactivates 10^6 microorganisms.

3.40 Repeat the test twice with fresh challenges.

3.41 If the inactivation of 10^6 microorganisms has been confirmed, determine the extent of treatment for the production sterilization process. This approach is best suited to sterilants that exhibit linear inactivation kinetics. In such cases, the extent of treatment can be defined conservatively as twice that employed in 3.37 hence the term half cycle validation.

3.42 In practice this work will have been undertaken by the sterilizer manufacturer as part of the EN ISO 14937 process. Hydrogen peroxide sterilization processes do not always exhibit straight line, time based logarithmic inactivation kinetics; especially where multi dynamic stages are used. Therefore it is common for these type of sterilizers to have two identical or equal lethality phases. Annex E 5.3.1 of EN 14937 discusses the microbicidal effectiveness of sterilizing agents.

3.43 Therefore when undertaking this test, the cycle should be aborted after the first phase or configured not to deliver any sterilant during the second phase.

3.44 Each manufacturer should provide their method for undertaking this test. However, whatever method is chosen, it should include the following requirements:

- be based on a half cycle process;
- use either a self contained biological indicator system, biological indicators or directly inoculated challenge devices. If biological indicators or direct inoculation is used, the recovery methods will require separate validation. Advice from a microbiologist should be sought in such cases;
- if not based upon direct inoculation of medical devices, incorporate a process challenge device to simulate a worst case challenge;
- incorporate 10^6 *Geobacillus stearothermophilus* spores;
- be undertaken 3 times for each operating cycle.

Ethylene oxide sterilization validation (using a contract sterilization company)

3.45 Since the efficacy of EO sterilization cannot be assured by the measurement of cycle variables, the only definitive performance tests currently available for EO sterilizers are microbiological. Chemical indicators are used to give an early indication of the efficacy of gas penetration but by themselves are not sufficient to validate the sterilization process. When selecting a sub-contract provider, assurances as to the extent and type of validation that has been performed should be sought. As a minimum, the validation undertaken should be in accordance with EN ISO 11135-1: 2014.

EO performance qualification

3.46 PQ tests are required for loading conditions representing every production load. Due to the wide variety of medical devices processed by EO, it is not always practicable to conduct PQ tests for every possible loading condition. The provider will likely have categorised load items by the degree to which they can absorb and retain moisture and EO, and then ensure that loads are made up of items in the same category.

3.47 The amount of microbial contamination (the bioburden) after cleaning may need to be determined as part of the performance qualification process. However this is not normally required for hospital type loads where a wide range of items are to be sterilized and gas exposure times are calculated to be more than sufficient to deal with the maximum anticipated bioburden (overkill method). Where such determinations are required though they should have been conducted in accordance with EN ISO 11737-1: 2018 'Sterilization of medical devices. Microbiological methods. Determination of a population of microorganisms on products'.

3.48 When procuring sub-contract sterilization, the provider should supply information regarding the PQ testing undertaken and its relationship to the medical devices you intend sending for processing.

4. Periodic testing

Schedule of periodic tests for ethylene oxide sterilizers

4.1 The periodic testing of the sub contractor's ethylene oxide sterilizers should be managed by them and be in compliance with EN 1422: 2014 'Sterilizers for medical purposes - Ethylene oxide sterilizers - Requirements and test methods'.

Schedule of periodic tests for hydrogen peroxide sterilizers

4.2 Periodic tests for hydrogen peroxide sterilizers should be carried out at daily, weekly, quarterly and yearly intervals or to a schedule specified by the sterilizer manufacturer. They are the shared responsibility of the Competent Person (Decontamination) (CP(D)) and the User.

4.3 The yearly test schedule should be identical to the revalidation schedule and should contain tests for recommissioning and when repeating performance qualifications.

4.4 Tests should be performed on completion of planned maintenance tasks, see section 6. Schedules for periodic tests for hydrogen peroxide sterilizers are shown, see Table 2. However it should be noted that these are the minimum tests required and that the testing should include all tests required to demonstrate compliance with EN ISO 14937: 2009 as recommended by the manufacturer. The hydrogen peroxide sterilizer standard EN 17180 was being developed in 2018. Once published this would become the appropriate standard for periodic testing of hydrogen peroxide sterilizers.

4.5 The calibration of thermometric test equipment should be checked in accordance with Part B of SHTM 01-01.

4.6 The results of the tests carried out by the CP(D) should be kept in the plant history file. The results of the tests carried out by the User should be kept in the sterilizer process log.

Hydrogen peroxide sterilizer - Daily test – User
Visually inspect the chamber interior noting condition of all parts. Ensure correct operation of shelves/runners. Inspect and clean door seal. Check sterilizer for visible signs of damage or wear. Check printer for paper (if fitted). Routine microbiological test for each production cycle type used if no IMS fitted (BI test).
Weekly tests – CP(D)
Daily tests. Any other weekly checks recommend by the manufacturer. Routine microbiological test for each cycle type used (BI test), see section 4.14. Automatic control test for each cycle type used, see section 4.7.
Quarterly tests – CP(D)

Weekly tests. Any other tests recommended by the manufacturer.
Yearly and revalidation tests – CP(D)
Yearly safety checks. Chamber integrity tests as defined by the manufacturer. Automatic control test for each cycle type (no load). Verification of calibration of both control and IMS instruments. Half cycle microbiological test with biological and chemical indicators within a process challenge device repeated 3 times for each cycle type fitted. Any additional tests to meet the manufacturers EN ISO 14937 regime. PQ production load test based upon half cycle test and biological indicators (if required).

Table 2: Minimum periodic tests for hydrogen peroxide sterilizers

Automatic control test

4.7 The automatic control test is designed to show that the operating cycle functions correctly as shown by the values of the cycle variables indicated and recorded by the instruments fitted to the sterilizer.

4.8 It should be carried out once a week and is one of the tests for ensuring that the sterilizer continues to function correctly.

Apparatus

4.9 For weekly tests place a production load in the chamber. If the test proves satisfactory, the sterilized load may be released for normal use. For validation and yearly/revalidation tests the chamber can be empty.

Method

4.10 Select the operating cycle to be tested. This should normally be the highest temperature compatible with the load. Start the cycle.

4.11 Ensure that a Batch Processing Record (BPR) is made by the recording instrument fitted to the machine.

Results

4.12 The test should be considered satisfactory if the following requirements are met:

- a visual display indicating “cycle complete” occurs;
- the values of the cycle variables, as indicated by the instruments on the machine or shown on the BPR, are within the limits established as giving satisfactory results either by the manufacturer or during PQ, during the whole of the operational cycle;
- during the plateau period determined from the recorded chamber temperature:
  - the indicated and recorded chamber temperatures are within the appropriate sterilization temperature band specified by the manufacturer;
  - the difference between the indicated, recorded and any other independent monitor chamber temperature does not exceed 2ºC;

  - the difference between the indicated, recorded and any other independent monitor chamber pressure does not exceed 0.1 bar;
- the door cannot be opened until the cycle is complete;
- the person conducting the test does not observe any mechanical or other anomaly.

4.13 Where an independent monitoring system is employed that has the necessary data-processing capability, process variability may be monitored automatically through presentation of suitable control charts displaying critical process data (for example, vacuum and pressure set points on each pulse, and average, minimum and maximum temperatures and pressures during the sterilization hold phase).

Routine microbiological test

Introduction

4.14 A routine microbiological test using a self contained biological indicator is required at least weekly on hydrogen peroxide sterilizers. If no independent monitoring system is fitted then the test should be undertaken at least daily. Some sterilizer manufacturers and some local CDU policies may require the use of a biological indicator with every production load. If in doubt as to the required frequency of this test, advice from the manufacturer and the AE(D) should be sought.

4.15 As mentioned previously in the design section, these will usually take the form of a self contained indicator which includes the chosen biological challenge (usually 10^6 *Geobacillus stearothermophilus* spores), the growth medium and packaging designed to protect the indicator through the process, keep the spores and growth medium separate until after processing and allow reading of the result without the need to open the challenge device.

4.16 In the absence of a published international standard, the manufacturer should specify the indicator system to be used. The self-contained BI should be packaged in a manner that is consistent with the medical devices being sterilized and use spores with equivalent resistance as the spores used for validation.

4.17 Chemical indicators are used to give an early indication of the efficacy of sterilant penetration but by themselves are not sufficient to monitor the sterilization process.

Method

4.18 Assemble the self contained biological indicators and chemical indicators as instructed by the manufacturer. Wrap as instructed (usually in a sterilization pouch). Place the recommended number (depending upon type and chamber size) in the chamber at the locations advised by sterilizer manufacturer. This should be the most challenging area for the sterilant to reach.

4.19 Select and start the operating cycle.

4.20 At the end of the cycle, remove the indicators from the load. Check that the chemical indicators show a uniform colour change. If so, process the biological indicator as instructed.

4.21 If the chemical indicators do not show a uniform colour change, then the test should be abandoned.

4.22 Use an unprocessed biological indicator as a control and incubate alongside the processed indicator.

4.23 The test is a pass if the processed indicators do not show any growth and the control indicator shows a fail.

5. Sterile product release

5.1 A procedure for sterile product release post sterilization should be specified. This procedure should define the criteria for designating a sterilization process as conforming to its specification. Parametric release should only be used if all process parameters are specified, controlled and directly monitored. Records of process parameters should be retained. If biological indicators or chemical indicators are used to monitor the sterilization process, the results from exposure to these indicators should be included within the criteria for sterile product release. If the criteria specified are not met, the product should be considered as non-conforming and handled in accordance with documented procedures. The Independent Monitoring System (IMS) data should also be considered.

The procedures should confirm the following:

- that the sterilizer has been loaded as local policies and in conjunction with the PQ specification;
- that the settings for the operating cycle were in accordance with the PQ specification;
- that the Batch Process Record (BPR) for the cycle conforms with the relevant Master Process Record (MPR) within the permitted tolerances (see previous paragraph);
- that any indicated readings needing to be noted during the cycle have been noted and are in accordance with the PQ specification;
- that the sterilized load shows no obvious anomalies, such as damaged packaging or containers, which could suggest a faulty cycle;
- the load items of packaged medical devices are visibly dry.

Hydrogen peroxide sterile product release procedure

5.2 The release of the sterile product should be on the basis of defined release criteria, which should include all or some of the following:
• satisfactory completion of a full cycle and the achievement of the defined process parameters including IMS data;
• satisfactory Biological Indicator (BI) or Process Challenge Device (PCD) test results;
• satisfactory product or package integrity/functionality including label information;
• any other tests as defined by internal quality procedures such as satisfactory H_2O_2 residual results.

Ethylene oxide sterile product release procedure

5.3 Before releasing the medical device(s) back to healthcare organisation, the sub-contract provider should review and approve all documentation for each sterilization load to ensure that process specifications have been met. This should form part of any Ethylene Oxide (EO) sterilization contract. The contract documentation should

include the requirement for the provider to include evidence of satisfactory product release with each processed medical device.

5.4 The sub-contract provider should approve the release of the product on the basis of their defined release criteria, which may include all or some of the following:

- satisfactory completion of a full cycle and the achievement of the defined process parameters;
- satisfactory BI or PCD test results;
- satisfactory product or package integrity/functionality including label information;
- any other tests as defined by internal quality procedures such as satisfactory EO residual results.

5.5 If there is mixing of devices from different customers within the same sterilization load, then the contract should include an obligation for alerting of all parties of any BI failures with any part of that load.

5.6 Although the product release will likely be performed by the sub-contract provider, the ultimate responsibility for use of the medical devices remains with the healthcare organisation. They should therefore develop their own procedures for approving the release of the sterile product following its return from the sub-contract EO sterilization.

6. Maintenance

Maintenance of equipment

6.1 Preventative maintenance should be planned and performed in accordance with documented procedures which are in line with the equipment manufacturer's instructions for use. The procedure for each planned maintenance task and the frequency at which it is to be carried out should be specified. Records of maintenance should be retained. Equipment should not be used to process product until specified maintenance tasks have been satisfactorily completed and recorded. The maintenance scheme, maintenance procedures and maintenance records should be reviewed periodically by a designated person. The results of the review should be recorded.

7. Guidance on safety risk assessment

Overview

7.1 As with all sterilization processes, specific safety risks must be taken into account. These include:

- safety of the patient, ensuring that no toxic residues remain or are formed on the medical device following the process and that sterility is reliably achieved;
- safety of staff using the process, including physical, ergonomic and chemical considerations;
- safety of the medical devices, ensuring that they are not damaged by the process;
- safety of the environment.

7.2 Factors to be considered in any local risk assessment include, but are not limited to:

- consideration of environmental and workplace exposure limits for the chemical agents used and any secondary products generated;
- appropriate application of environmental and personal monitoring. This is essential for some sterilization agents. Consideration should be given to monitoring whenever toxic gases or vapours are employed. In some instances, equipment may contain monitoring devices. The assessment should include the possible use of non-machine integrated monitors and alarms;
- consideration to degassing associated hazards and the environments used in processing and storage;
- containment and ventilation associated with the work environment;
- constraint of splash and aerosol hazards from liquid agents in use, including hydrogen peroxide;
- the use of secondary containment combined with negative pressure exhaust ventilation should be considered and may be an HSE requirement for some of the technologies.

7.3 Safety risk assessment should be applied to all decontamination technologies, regardless of type or status. The COSHH regulations should be followed.

Sterilant exposure levels

7.4 Workplace exposure limits are published by the Health and Safety Executive (HSE) for some of the chemicals involved in low temperature sterilization. Long term and short term exposure limits are specified for Ethylene oxide and for hydrogen peroxide. See Table 3.

Sterilant	Long-term exposure limit (8-hr TWA reference period) ppm	Short-term exposure limit (15 minute reference period) ppm	The Carc, Sen and Sk notations identified in IOELV Directives[2]
Ethylene Oxide	5	-	Carc
Hydrogen Peroxide	1	2	

Table 3: Exposure limits from EH40 published by the Health and Safety Executive (Health and Safety Executive, 2011)

7.5 Care should be taken regarding medical device package degassing after sterilization, where process chemicals may be retained in the processed medical device pack and eluted afterwards. This should form part of any local risk assessment.

[2] Carc Capable of causing cancer and/or heritable genetic damage.
Sen Capable of causing occupational asthma.
Sk Can be absorbed through the skin. The assigned substances are those for which there are concerns that dermal absorption will lead to systemic toxicity.

8. Medical device compatibility

8.1 The compatibility of the process with the medical devices for which it is intended to sterilize is a key consideration when choosing alternative sterilization technology. Sterility does not necessarily mean compatibility. The advice of both the sterilizer and the medical device manufacturers should be sought when considering low temperature sterilization methods; it should be ensured that the requirements of both can be reconciled.

8.2 There is a lack of definition for test methods and protocols. This makes assessment of sterility and compatibility potentially more difficult compared to steam sterilization. This problem is compounded by the fact that seemingly similar processes can operate very differently. This is particularly the case with hydrogen peroxide sterilizers due to the lack of both an equipment and validation standard.

8.3 It is a requirement of the Medical Device Regulation (EU) 2017/745 for manufacturers of medical devices to provide adequate instructions for use which includes reprocessing information. The User should consult the manufacturer's instructions for use including the compatibility of medical devices that can be processed in the sterilizer. Policies and procedures controlling the use of low temperature sterilization methods should be developed in conjunction with the relevant manufacturer's instructions for use.

8.4 EN ISO 17664: 2017 gives advice to medical device manufacturers on the required content of processing instructions. It can serve as a useful guide for Users as to what should be expected from compliant processing instructions.

8.5 When medical devices are only compatible with low temperature processes, the information provided can be much more specific than with steam processes. It is not unusual to see a specific make or model of sterilizer specified in the instructions for use. This limits the choice of method and often a CDU will need to consider its existing medical device types when purchasing a low temperature sterilizer.

8.6 EN ISO 14937: 2009 gives advice on the roles and responsibilities in this area within Annex E, see Figure 2.

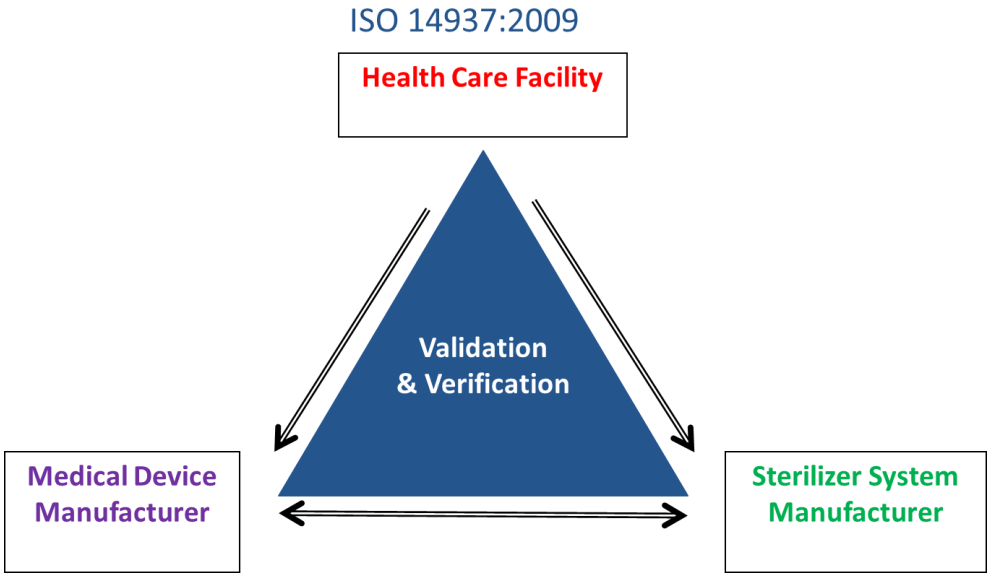


Figure 2: Allocation of responsibilities in EN ISO 14937: 2009

Note: Allocation of responsibilities in EN ISO 14937: 2009.

The sterilizer manufacturer has developed the specification for the sterilizer.

The CDU should review the equipment specification in conjunction with the sterilizer manufacturer to confirm that they have the infrastructure necessary to operate the sterilization equipment.

The CDU has identified the medical devices that it intends to reprocess in the sterilizer.

The instructions for reprocessing these medical devices are provided by the medical device manufacturer and include appropriate instructions for cleaning, disinfection and sterilization.

The medical device manufacturer has undertaken studies in collaboration with the sterilizer manufacturer in order to validate the reprocessing instructions provided.

The health care facility should review the data on the effectiveness of its cleaning processes and confirms they are adequate for the particular medical device(s) and sterilization process.

The sterilizer manufacturer and the medical device manufacturer have collaborated to define the sterilization process for the particular medical devices and have included the relevant instructions within each of their instructions for use.

The CDU should review the documentation and confirm that it has the capability and equipment to follow these instructions.

8.7 It is the responsibility of medical device suppliers to inform Users of compatible decontamination processes. Only those processes deemed compatible by the manufacturer of the medical device should be used.

Lumen claims by the sterilizer manufacturer

8.8 One of the primary benefits of a low temperature sterilization processes is the ability to sterilize some flexible endoscopes. Users should be aware that each low temperature sterilizer manufacturer may make different claims regarding the ability of their sterilizer to sterilize medical devices comprising of lumens. The length (maximum) and diameter (minimum) of lumens that can be processed should be stated by the sterilizer manufacturer.

References

These references were current at the time this document was produced. Anyone using this document should ensure that they refer to the current versions of any references.

Standards

EN 868 -6: 2017 Paper for low temperature sterilization processes — Requirements and test methods. CEN.

EN 868 -7: 2017 Adhesive coated paper for low temperature sterilization processes — Requirements and test methods. CEN.

EN 1422: 2014 Sterilizers for medical purposes - Ethylene oxide sterilizers - Requirements and test methods. CEN.

EN ISO 10993-7: 2008 - Biological evaluation of medical devices. Part 7: Ethylene oxide sterilization residuals. CEN.

EN ISO 10993-17: 2009 - Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances. CEN.

EN ISO 11135-1: 2014 - Sterilization of health care products — Ethylene oxide — Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices. CEN.

EN ISO 11138-1: 2017 - Sterilization of health care products — Biological indicators Part 1: General requirements. CEN.

EN ISO 11138-2: 2017 - Sterilization of health care products - Biological indicators for ethylene oxide sterilization processes. CEN.

EN ISO 11140-1: 2014 - Sterilization of health care products — Chemical indicators Part 1: General requirements. CEN.

EN ISO 11737-1: 2018 - Sterilization of medical devices. Microbiological methods. Determination of a population of microorganisms on products. CEN.

EN ISO 13485: 2016 - Medical devices. Quality management systems. Requirements for regulatory purposes. CEN.

EN ISO 14937: 2009 - Sterilization of health care products. General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices. CEN.

EN ISO 14161: 2009 - Sterilization of health care products - Biological indicators - Guidance for the selection, use and interpretation of results. CEN.

EN ISO 14971: 2012 - Medical devices. Application of risk management to medical devices. CEN.

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EN 1717: 2000 - Protection against pollution of potable water in water installations and general requirements of devices to prevent pollution by backflow. CEN.

EN ISO 18472: 2006 - Sterilization of health care products. Biological and chemical indicators. Test equipment and methods. CEN.

EN 60601-1-2: 2015 - Medical electrical equipment. General requirements for basic safety and essential performance. Collateral Standard. Electromagnetic disturbances. Requirements and tests.

EN 61010-1: 2010 - Safety requirements for electrical equipment for measurement, control, and laboratory use. General requirements.

EN 61010-2-040: 2015 - Safety requirements for electrical equipment for measurement, control, and laboratory use. Particular requirements for sterilizers and washer-disinfectors used to treat medical materials.

IEC 61010-2-120: 2016 - Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 2-120: Particular safety requirements for machinery aspects of equipment.

Healthcare guidance and publications

Scottish Health Planning Note 13 Part 1:2011 – Central Decontamination Unit

Scottish Health Technical Memorandum (SHTM) 01-01 Decontamination of medical devices in a Central Decontamination Unit - Part A: Management, 2018.

Scottish Health Technical Memorandum (SHTM) 01-01 Decontamination of medical devices in a Central Decontamination Unit - Part B: Test Equipment/Methods, 2018.

Scottish Health Technical Memorandum (SHTM) 01-01 Decontamination of medical devices in a Central Decontamination Unit - Part C: Sterilization by steam, 2018.

Scottish Health Technical Memorandum (SHTM) 01-01 Decontamination of medical devices in a Central Decontamination Unit - Part D: Automated cleaning and disinfection, 2018.

Scottish Health Technical Memorandum (SHTM) 01-01 Decontamination of medical devices in a Central Decontamination Unit - Part F: Inspect, assemble and package, 2018.

Scottish Health Technical Memorandum 04-01 – 'Water safety for healthcare premises', 2014.

Regulation

Control of substances hazardous to health (COSHH) Regulations: 2002

Electromagnetic Compatibility Regulations: 1992

Pressure Equipment Regulations: 1999

Provision and Use of Work Equipment Regulations: 1998 (amended by the Health and Safety (Miscellaneous Amendments) Regulations 2002 and the Health and Safety (Miscellaneous Repeals, Revocations and Amendments) Regulations 2013)

Workplace (Health, Safety and Welfare) Regulations: 1992

The Public Water Supplies (Scotland) Regulations: 2014

Water Supply (Water Fittings) (Scotland) Byelaws: 2014

Standards under development in 2018

ISO/DTS 19572: Sterilization of health care products -- Guidance on the application of ISO14937 to the sterilization of medical devices using Ethylene Oxide in a flexible sterilization chamber.

ISO/CD 16342: Sterilization of health care products -- Biological indicators -- Method for validation of a biological indicator incubation period.

ISO/NP 11138-6: Sterilization of health care products -- Biological indicators -- Part 6: Biological indicators for hydrogen peroxide sterilization processes.

prEN 17180: Dec 2017 Consultation draft - Sterilizers for medical purposes - Low temperature vaporized hydrogen peroxide sterilizers - Requirements and testing.

ISO/NP 22441 Sterilization of health care products -- Low temperature vaporized hydrogen peroxide -- Requirements for the development, validation and routine control of a sterilization process for medical devices.