TECHNICAL SPECIFICATION

ISO/TS 11135-2

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Sterilization of health care products — Ethylene oxide —

Part 2: Guidance on the application of ISO 11135-1

Stérilisation des produits de santé — Oxyde d'éthylène — Partie 2: Directives relatives à l'application de l'ISO 11135-1

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

In other circumstances, particularly when there is an urgent market requirement for such documents, a technical committee may decide to publish other types of document:

— an ISO Publicly Available Specification (ISO/PAS) represents an agreement between technical experts in an ISO working group and is accepted for publication if it is approved by more than 50 % of the members of the parent committee casting a vote;

— an ISO Technical Specification (ISO/TS) represents an agreement between the members of a technical committee and is accepted for publication if it is approved by 2/3 of the members of the committee casting a vote.

An ISO/PAS or ISO/TS is reviewed after three years in order to decide whether it will be confirmed for a further three years, revised to become an International Standard, or withdrawn. If the ISO/PAS or ISO/TS is confirmed, it is reviewed again after a further three years, at which time it must either be transformed into an International Standard or be withdrawn.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO/TS 11135-2 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

ISO/TS 11135-2, together with ISO 11135-1, cancels and replaces ISO 11135:1994 and ISO 11135/Cor.1:1994, which have been technically revised.

ISO/TS 11135 consists of the following parts, under the general title *Sterilization of health care products — Ethylene oxide*:

— *Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

— *Part 2: Guidance on the application of ISO 11135-1*

Introduction

This Technical Specification describes some of the methods that may be employed to achieve the requirements contained in ISO 11135-1. This document is not intended as a checklist for assessing compliance with ISO 11135-1, rather it is intended to promote a uniform understanding and implementation of ISO 11135-1 by providing explanations and possible methods for achieving compliance with specified requirements. It highlights important aspects and provides examples.

This Technical Specification addresses ethylene oxide (EO) sterilization in both the industrial and health care facility settings, and it acknowledges the similarities and differences between the two applications.

Among the similarities are the common need for quality systems, staff training, and proper safety measures. The major differences relate to the unique physical and organizational conditions in health care facilities, and to the initial condition of re-usable devices being presented for sterilization.

Health care facilities differ from medical device manufacturers in the physical design of processing areas, in the equipment used, and in the availability of personnel with adequate levels of training and experience. The primary function of the health care facility is to provide patient care; medical device reprocessing is just one of a myriad of activities that are performed to support that function.

In terms of the initial condition of medical devices, medical device manufacturers generally sterilize large numbers of similar devices that have been produced from virgin material. Health care facilities, on the other hand, must handle and process both new medical devices and re-usable medical devices of different descriptions and with varying levels of bioburden. They are therefore faced with the additional challenges of cleaning, evaluating, preparing and packaging a medical device prior to sterilization. In this document, alternative approaches and guidance specific to health care facilities are identified as such.

In general, moist heat sterilization (also known as steam sterilization) is the method of choice for medical devices and supplies that are sterilized in health care facilities. However, EO gas and its mixtures are effective sterilants that are primarily used for heat- and moisture-sensitive medical devices that cannot be steam sterilized.

For ease of reference, the numbering in this technical specification corresponds to that in ISO 11135-1.

Sterilization of health care products — Ethylene oxide —

Part 2:
Guidance on the application of ISO 11135-1

1 Scope

This Technical Specification provides guidance for the requirements in ISO 11135-1:2007. It does not repeat the requirements and is not intended to be used in isolation.

The exclusions in ISO 11135-1 apply also to this Technical Specification.

For ease of reference, the clause numbering in this Technical Specification corresponds to that in ISO 11135-1:2007. Further guidance for the requirements given in ISO 11135-1 is also included in Annex C of ISO 11135-1:2007 and should be used in conjunction with this Technical Specification.

This guidance document is intended for people who have a basic knowledge of the principles of EO sterilization but may need help in determining how to best meet the requirements contained in ISO 11135-1. This document is not intended for people lacking a basic knowledge of the principles of EO sterilization.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 11135-1:2007, *Sterilization of health care products — Ethylene oxide — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO 11138-2:2006, *Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes*

ISO 11140-1:2005, *Sterilization of health care products — Chemical indicators — Part 1: General requirements*

ISO 11737-1, *Sterilization of medical devices — Microbiological methods — Part 1: Determination of a population of microorganisms on products*

ISO 13485:2003, *Medical devices — Quality management systems — Requirements for regulatory purposes*

ISO 17664, *Sterilization of medical devices — Information to be provided by the manufacturer for the processing of resterilizable medical devices*

3 Terms and definitions

For the purposes of this document, the terms and definitions in ISO 11135-1 and the following apply.

3.1
dunnage
material used to mimic all or part of a sterilization load

3.2
health care facility
set of physical infrastructure elements intended to support the delivery of specific health-related services

3.3
processing group
collection of products or product families that can be sterilized in the same EO sterilization process

NOTE All products within the group have been determined to present an equal or lesser challenge to the sterilization process than the challenge device for that group.

3.4
EO product family
collection of products that are determined to be similar or equivalent for validation purposes

3.5
re-usable medical device
medical device designated or intended by the manufacturer as suitable for reprocessing and re-use

NOTE This is not a medical device that is designated or intended by the manufacturer for single use only.

3.6
single use medical device
medical device that is designated or intended by the manufacturer for one-time use only

3.7
sterilization specialist
person with knowledge of the sterilization technology being utilized and its effects upon materials and microorganisms

NOTE This level of knowledge has been obtained by both practical and theoretical means and the person does not require guidance on the basic principles of the technology involved.

4 Quality management systems

4.1 Documentation

4.1.1 No guidance offered.

4.1.2 No guidance offered.

4.2 Management responsibility

4.2.1 Each organization should establish procedures for identifying training needs and ensure that all personnel are trained to adequately perform their assigned responsibilities.

4.2.2 No guidance offered.

4.3 Product realization

4.3.1 Purchasing procedures in a health care facility should ensure that re-usable medical devices are supplied with validated instructions for cleaning, disinfection, sterilization and aeration as specified in ISO 17664.

4.3.2 For those facilities that do not fully comply with ISO 13485, such as health care facilities, procedures for identification of product and maintenance of traceability, should include the labelling of each item or package prior to sterilization with a lot control identifier that includes the following information:

a) the sterilizer ID or code;

b) the date of sterilization;

c) the cycle number (i.e. the cycle run of the day or sterilizer).

It is recommended that the identity of the person who assembled the pack also be included on the identifier, to allow for further investigation if a problem should arise.

Lot identification information enables personnel to retrieve items in the event of a recall and to trace problems to their source.

4.3.3 No guidance offered.

4.4 Measurement, analysis and improvement — Control of non-conforming product

No guidance offered.

5 Sterilizing agent characterization

5.1 Sterilizing agent

EO is a highly penetrative gas that will permeate most packaging materials and polymeric materials. Widely recognized compositions include 100 % EO and blends with carbon dioxide or nitrogen. The storage conditions for EO should be in accordance with the EO manufacturer's recommendations and all applicable regulations.

5.2 Microbicidal effectiveness

No guidance offered.

5.3 Materials effects

No guidance offered.

5.4 Environmental considerations

5.4.1 EO is toxic, flammable and explosive; therefore, extreme caution should be used during its storage, handling and use.

5.4.2 Effluent gas should be discharged through an EO-gas treatment system, such as a catalytic oxidiser, wet acid scrubber or thermal oxidiser.

When choosing a diluent, its ozone depleting potential should be taken into consideration.

6 Process and equipment characterization

In health care facilities, process and equipment characterization are generally the responsibility of the sterilizer manufacturer. The management of the health care facility should have controls in place to ensure that its equipment purchases conform to national, regional and local regulations and are suitable for the products intended to be sterilized. The management of the health care facility should ensure the facility has the infrastructure necessary to operate the sterilizing equipment and to achieve sterilization of medical devices.

6.1 Process characterization

No guidance offered.

6.2 Equipment characterization

6.2.1 The following factors should be considered when characterizing the equipment.

Preconditioning equipment characterization

Preconditioning may be performed in a separate preconditioning area (chamber, cell or room). The preconditioning area (if used) should have the following performance and monitoring capabilities:

— air circulation system: adequate air circulation to ensure the uniformity of temperature and humidity in the usable space, and to ensure that uniformity is maintained in a fully loaded room or chamber;

— airflow detection equipment, alarm systems or indicators monitoring the circulation system to ensure conformance to predetermined tolerances;

— means of monitoring temperature and humidity;

— means of controlling temperature and humidity;

NOTE Temperature and humidity sensor control systems may utilize redundant sensors for temperature and humidity determination in the room.

— a time clock or other means of recording time of load entry into and removal from the preconditioning area, if applicable.

Sterilization chamber equipment characterization

The sterilization chamber should have the following performance and monitoring capabilities:

— means of monitoring chamber pressure, temperature and humidity (if humidity additions are controlled by sensor readings);

— means of controlling chamber pressure, temperature and humidity, if humidity additions are controlled by sensor readings [when sensors are fixed on the equipment, ensure that a correlation is made during installation qualification (IQ) or operational qualification (OQ) at the coldest location];

— if parametric release is used, instrumentation for the direct analysis of humidity during conditioning and EO concentration during sterilant exposure time;

— a system controlling that gaseous EO was admitted to the chamber. This can be done by measuring the temperature of the EO gas flowing from the vaporizer to the sterilizer chamber or monitoring the pressure rise during EO injection. This system may control EO concentration during sterilant exposure time.

Aeration equipment characterization

An aeration area (chamber, cell or room) may be used to remove EO residuals from product/packaging. Temperature uniformity, fresh air make-up and air re-circulation throughout the area are important to ensure consistent and reproducible results. The aeration area should have the following:

— airflow detection equipment, alarm systems or indicators monitoring the air handling system to ensure that it operates within specified parameters and maintains adequate airflow in a fully loaded room or chamber;

— equipment to re-circulate air;

— means of monitoring room temperature;

— means of controlling room temperature.

Prior to removing product from a sterilizer, precautions should be taken to ensure that operators are not exposed to high levels of EO due to the outgassing of the load.

The equipment specification should be reviewed to ensure that regulatory and safety requirements are met, technical specifications are appropriate, and services and infrastructure necessary to operate the equipment are available.

6.2.2 Humidification by steam injection is required in ISO 11135-1, because humidifiers that operate by dispersion of unheated water as an aerosol (e.g. spinning disc humidifiers and nebulizers) can be potent sources of microbial contamination.

6.2.3 No guidance offered.

6.2.4 If there is an undetected failure of a control or monitoring function, a sterilization load could be released without having met its required processing parameters. To prevent this from happening, it is general practice to have redundant sensors for many critical process parameters. The common options for utilizing these redundant sensors include:

a) use one sensor for control, and another sensor for monitoring and reporting;

b) use two sensors, or their average value, for both monitoring and control; this system needs to generate an automatic fault condition if the difference between the two sensors exceeds a defined value;

c) use dual element sensors for both monitoring and control; this system needs to generate an automatic fault condition if the difference between the two elements exceeds a defined value.

7 Product definition

7.1 General

Product definition involves documentation of essential information about the medical device to be sterilized (i.e. the new or modified product).

7.1.1 Product definition for a medical device includes the medical device itself, the primary package containing the device, and any accessories, instructions, or other items included in the primary package. It also includes a description of the intended functionality of the medical device, and the available manufacturing and sterilization processes. The product definition process should also consider whether this is a new design, or whether it is part of an existing EO product family.

The following should be considered as part of product definition:

a) physical description of the medical device (composition and configuration);

b) intended use of the medical device;

c) whether the medical device is intended for single use or for multiple use;

d) design characteristics that would affect the choice of sterilization process (e.g. batteries, fibre-optics, computer chips);

e) raw materials/manufacturing conditions that could affect microbiological quality (e.g. materials of natural origin);

f) required sterility assurance level (SAL);

g) packaging;

h) loading pattern; requirements for a specific load or mixed loading patterns, or range of acceptable loading patterns;

i) compatibility with the sterilant gas or gas mixture and EO processing conditions (preconditioning, sterilization and aeration processes).

7.1.2 A technical review should be performed to compare the new or modified product to the validated product and/or process challenge device (PCD) that was used to validate the existing EO process. The construction and configuration of the new or modified product should be carefully examined for any features that could present obstacles to the penetration of EO, heat or humidity. For medical device manufacturers, this comparison should also involve an examination of factors that could affect the initial bioburden on the product, including the location of the manufacturing facilities, the types of raw material used, the sources of these materials and production methods. For new re-usable products, this comparison should include the evaluation of the cleaning efficacy for this product.

If a new or modified product is demonstrated to be equivalent to an existing medical device or PCD for which sterilization characteristics are already known, the new or modified product might be considered to be part of an EO product family or a processing group.

NOTE AAMI TIR28[10] is a useful guide for minimizing the risk of introducing a new or modified product that presents a greater challenge to the sterilization cycle than was previously validated.

As part of the technical review the following questions should be considered. If the answer to any of the following questions is “yes,” further evaluation of the new or modified product might be necessary to determine if it is more difficult to sterilize than the previously validated product:

a) With respect to the previously validated product, does the new or modified product:

1) have more restricted passageways or inner chambers;

2) have fewer openings;

3) have more internal surfaces;

4) have more mated surfaces;

5) have more closures;

6) have longer or narrower lumens;

7) include changes or differences that could reduce the transfer of heat, moisture or sterilant gas;

8) have a bioburden number or resistance significantly higher than that of the reference product (due to manufacturing conditions, handling, cleaning process or materials used) or

9) contain materials or structures that could be adversely affected by the proposed processing or sterilization method?

b) With respect to the previously validated product, does the packaging of the new or modified product:

1) have any changes in packaging elements, including instructions or protective barriers;

2) have any additional impermeable protective barriers, e.g. container, case, template, that would restrict or interfere with sterilant or humidity penetration or removal;

3) have a change in the porosity of the packaging material (e.g. basis weight, coating, treatment – adhesive or coating on paper);

4) have a decrease in the surface area of the venting material or underlying opening, e.g. application of tape or secondary label, change in size of label;

5) increase the bioburden level of the product or

6) change the number of barrier layers?

c) With respect to the previously validated product, does the load configuration of the new or modified product:

1) differ significantly from the validated load configuration of the reference load;

2) differ significantly in the amount of absorptive materials;

3) differ significantly in density from that of the reference load or

4) differ significantly in total load volume?

7.1.3 No guidance offered.

7.1.4 No guidance offered.

7.1.5 A means of demonstrating equivalence is the comparison of the relative rates of inactivation of BIs placed in the most difficult-to-sterilize location within the new or modified product and previously validated product when both are exposed to a fractional cycle.

A PCD is a device or test pack into which a microbiological challenge is located. Examples of ways to develop PCDs for use in the demonstration of equivalence include, but are not limited to:

a) placement of a microbiological challenge between rings, lands, grommets or ribs of a syringe stopper;

b) placement of a microbiological challenge in the middle of the lumen of a tube that is then reconnected using a solvent bond agent or a connector to restore product integrity;

c) placement of a microbiological challenge in an interface;

d) placement of a microbiological challenge in a series of envelopes or packages.

Several PCD designs have been recommended for use in health care facilities.

NOTE 1 For further information see EN 1422[13], ANSI/AAMI ST41[11] and AS/NZS 4187[12].

To prepare the PCD, the microbiological challenge can be inoculated on the product either directly or indirectly. Direct inoculation is accomplished by applying a liquid suspension of the spores on the product. Indirect inoculation is accomplished by placing an inoculated carrier either within the package or in/on the product.