TECHNICAL SPECIFICATION

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Sterilization of medical devices — Guidance on the requirements for the validation and routine processing of ethylene oxide sterilization processes using parametric release

Stérilisation des dispositifs médicaux — Lignes directrices concernant les exigences de validation et de traitement de routine des procédés de stérilisation à l'oxyde d'éthylène par libération paramétrique

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

ISO 11135 includes requirements for development, validation and routine control of ethylene oxide (EO) sterilization processes. This document is intended to be used in conjunction with ISO 11135.

ISO 11135:2014:11.1 refers to criteria for designating conformity of the sterilization process used for a particular sterilization load as including:

a) confirmation that the data recorded during routine processing meet the sterilization process specification;

b) confirmation of no growth of the test organism for any biological indicator (BI) (if used).

Parametric release is the declaration of adequacy of routine processing for a validated sterilization process based solely on measurement and documentation of physical process parameters rather than results of BIs, therefore b) does not apply.

The term BI release is used when the declaration of adequacy of the validated sterilization cycle includes a requirement for no growth in BIs exposed to that cycle.

The guidance in this document is informative and is not intended as a checklist for auditors. The guidance in this document provides examples of methods considered to be suitable as a means for conforming with the requirements of ISO 11135.

NOTE Sterilization in health care facilities differs from industrial sterilization, for example, the design of processing areas, control of product bioburden, access to relevant expertise in EO sterilization and sterilization equipment that might not be equipped to enable consideration of parametric release.

This guidance is intended for people who have knowledge of the principles of EO sterilization. Methods other than those given in the guidance can be used if they are effective in achieving conformity with the requirements of ISO 11135.

Sterilization of medical devices — Guidance on the requirements for the validation and routine processing of ethylene oxide sterilization processes using parametric release

1 Scope

This document provides guidance on the requirements of ISO 11135 that apply when parametric release is used to release the product after exposure to the sterilization process. It provides a path for transition of existing cycles, as well as a path for the development and implementation of a parametric release specification for a new cycle. Additionally, it highlights the importance and interrelationship of other process factors, i.e. load configuration and equipment performance, which influence reproducibility of an ethylene oxide (EO) sterilization process.

NOTE For ease of reference, the numbering of clauses in this document corresponds to that in the normative parts of ISO 11135.

No additional guidance is offered for processes where the declaration of adequacy of the validated sterilization cycle includes a requirement for no growth in biological indicators (BIs) exposed to that process.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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 11135:2014, *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 11135:2014 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

3.1
absolute humidity
AH
measure of water vapour in the air, regardless of temperature

Note 1 to entry: It is expressed as grams of moisture per cubic metre of air (g/m^3).

[SOURCE: ISO 11139:2018, 3.136.1]

3.2
gas concentration
weight of a specific gas in a given volume

Note 1 to entry: Concentration can be expressed as mg/l or g/m^3.

[SOURCE: ISO 11139:2018, 3.125]

3.3
humidity
measure of water vapour present in a gas

Note 1 to entry: Humidity is usually expressed as *absolute humidity* (3.1) (i.e. vapour pressure density), *relative humidity* (3.4) or dew point.

[SOURCE: ISO 11139:2018, 3.136]

3.4
relative humidity
RH
humidity relative to the maximum for a given temperature

Note 1 to entry: It is expressed in per cent.

[SOURCE: ISO 11139:2018, 3.136.2, definition modified.]

4 Quality management systems

No additional guidance specified or given.

5 Sterilization agent characterization

No additional guidance specified or given.

6 Process and equipment characterization

6.1 General

No additional guidance specified or given.

6.2 Process characterization

No additional guidance specified or given.

6.3 Equipment characterization

6.3.1 No additional guidance specified or given.

6.3.2 Additional guidance specified or given.

a) No additional guidance specified or given.

b) No additional guidance specified or given.

c) No additional guidance specified or given.

d) The equipment used for the measurement of temperature, EO and humidity should be specified.

NOTE 1 See also ISO 10012.

In addition to the requirements specified in ISO 11135:2014, Clause 10, equipment should monitor and record the following parameters for parametric release:

— chamber humidity by direct measurement, during conditioning;

— chamber EO concentration by direct measurement, at intervals throughout EO exposure;

— data from a minimum of two independent temperature sensors placed in different locations.

The monitoring and recording systems should be defined, characterized and documented for each parameter.

The location(s) of temperature, humidity and EO sensors or measuring devices should represent the conditions in the chamber.

1) Humidity

Humidity can be measured as either RH or AH. RH sensors typically use capacitive thin film technology and measure vapour pressure density at a given temperature. AH is a measure of the water concentration in a given volume of air and can be measured using spectroscopic technology. It can be measured with either a fixed sensor, via a sampling port in the chamber or with a data logger.

NOTE 2 RH can be determined by direct measurement or calculated from AH data.

Electronic sensors (e.g. capacitive thin film sensors) for measuring and recording (RH) can be calibrated using saturated salt solutions or qualified RH generation systems.

NOTE 3 It is common to report humidity as RH which can be determined by direct measurement or calculation when AH is directly measured.

RH sensors can be readily verified as being within their calibrated tolerances by comparing with a reference sensor that is traceable to a national standard.

Exposure to EO can impact the accuracy of some humidity sensors, resulting in them falling outside their calibrated tolerance. This may require more frequent calibration or verification of these sensors. Alternatively, they may be treated between uses or isolated during EO exposure to avoid potential adverse effects on the sensor.

2) EO concentration

For EO concentration measurement systems, the accuracy and precision should be known and documented.

There are two commonly used technologies employed for measurement of EO concentration: spectroscopic and gas chromatography (GC).

Spectroscopic technology measures the EO concentration by infrared (IR) light absorption of the EO molecule. Gas chromatographic technology measures the EO concentration against a standard curve after separation by an appropriate chromatographic column.

Measurement can be carried out either internally or externally. However, where the measurement of the EO concentration is being carried out external to the chamber the following additional aspects should be considered:

— length of pipework to the measurement sensor;

— compatibility of pipework to EO, for example appropriate grade of stainless steel;

— potential for leakage at connection points;

— heat tracing of pipework to minimize risk of condensation of EO or water vapour;

— mechanism for extracting the EO from the chamber, for example pump or blower.

3) Temperature

The type of equipment used for temperature monitoring is the same for both parametric or BI release, but two separate monitoring locations are required for parametric release. If the data from the sensors are averaged, then these sensors should be of the same type (e.g. thermocouple, thermistor, RTD probe) and have the same precision and accuracy.

e) No additional guidance specified or given.

f) No additional guidance specified or given.

g) No additional guidance specified or given.

6.3.3 No additional guidance specified or given.

6.3.4 No additional guidance specified or given.

6.3.5 No additional guidance specified or given.

7 Product definition

7.1 General

7.1.1 No additional guidance specified or given.

7.1.2 No additional guidance specified or given.

7.1.3 No additional guidance specified or given.

7.1.4 No additional guidance specified or given.

7.1.5 Load configuration should be specified and controlled.

Product, packaging materials, load density and configuration can impact EO concentration, humidity and temperature of the sterilization load.

7.1.6 No additional guidance specified or given.

7.2 Product safety, quality and performance

No additional guidance specified or given.

7.3 Microbiological quality

No additional guidance specified or given.