TECHNICAL SPECIFICATION

ISO/TS 21387

First edition
2020-09

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

Reference number
ISO/TS 21387:2020(E)

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Published in Switzerland

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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).

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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.

8 Process definition

8.1 Specifications for humidity and EO concentration can be established based on the analysis of the data gathered during process development or performance qualification (PQ).

The minimum specifications for humidity and EO concentration can be established based on data gathered during the microbiological performance qualification (MPQ) and physical performance qualification (PPQ) studies.

The maximum EO concentration specification should be established to ensure that product safety, quality and performance is not compromised (see ISO 11135:2014, 7.2 and ISO 10993-7).

Additional PQ may be needed to establish the appropriateness of the process parameters and their tolerances for parametric release. After PQ, the process specification includes the process parameters and their tolerance for each parameter.

NOTE The specification for other parameters including, but not limited to, temperature, pressure and time, can be established in the same manner for both parametric and BI release processes.

8.2 No additional guidance specified or given.

8.3 No additional guidance specified or given.

8.4 No additional guidance specified or given.

8.5 No additional guidance specified or given.

8.6 No additional guidance specified or given.

8.7 No additional guidance specified or given.

8.8 No additional guidance specified or given.

8.9 No additional guidance specified or given.

9 Validation

9.1 General

9.1.1 No additional guidance specified or given.

9.1.2 No additional guidance specified or given.

9.1.3 No additional guidance specified or given.

9.1.4 Additional PQ cycles can be performed to demonstrate the physical and microbiological performance reproducibility. This might involve designing cycles to deliver the process parameters for humidity, temperature and EO concentration at the established lower specification limit to confirm achievement of the required SAL and at the established upper specification to assess product or packaging functionality and EO residues.

9.2 Installation qualification

9.2.1 Equipment

9.2.1.1 Additional guidance specified or given.

a) Temperature measurement

The requirement to measure temperature within the sterilizer from a minimum of two locations is established to ensure that an undetected fault in a temperature sensor does not lead to the inadvertent release of an improperly processed load. If there is a difference in the two temperature data points, the acceptable temperature difference should be defined within the processing specification.

b) Humidity measurement

Direct analysis of the head space for RH can be performed using electronic sensors, GC, IR or other spectroscopic methods currently available to indicate water vapour concentration. The benefit of these methods is the real-time indication throughout the conditioning phase.

Electronic sensors require periodic calibration to offset the effect of exposure to the EO gas and can require replacement, heat treatment of the electronic sensors or more frequent calibration after repeated exposures to EO due to irreversible deterioration of materials currently utilized as sensing elements.

c) EO concentration measurement

The frequency of analysis required to demonstrate that the EO concentration process parameters and their tolerances are maintained throughout exposure time should be established during the PQ studies. Monitoring throughout the exposure time period should also be done as part of the validation, to determine how the EO concentration changes over time. The results of this analysis are specific to the product and load configuration being analysed. The analysis performed during the PQ study will result in documented specifications for how often direct analysis should be performed during routine processing.

As required in ISO 11135:2014, 9.5.5, the number of defined intervals for EO concentration sampling should be sufficient so that there is verification that the EO concentration will be within specification throughout EO exposure. This could be as few as two samples, with one taken after the end of gas injection or defined equilibration period and a second prior to sterilant removal. Typically, the number of samples is greater, for example when gas make-ups are used. Where an inert gas addition is included after EO injection, the ability to capture EO concentration data at the end of injection should be considered.

To ensure that the readings are representative of conditions within the chamber, it is important to consider a number of factors, including but not limited to:

— Location: it is important to ensure that the sensor(s) or the sampling location(s) for EO concentration, humidity and temperature measurement are representative of the environment in the chamber. If the sensors or sampling points are located within the recirculation system (if used), they should be placed in a location avoiding excessive turbulence.

— Water condensation: sensors or sampling point should be oriented in a manner to avoid any risk of build up or water condensation on the reading head of the sensor.

— Pressure influence: the measurement instrument should compensate for the impact of changing pressures (if applicable).

— Temperature uniformity: sensors, sampling points or sample piping for EO concentration and humidity might need to be either at or above the specified process temperature to give accurate readings. To achieve this, the sensor, piping or both might require heating. Measuring equipment should be located such that the maximum values of temperature and humidity specified for them

are not exceeded. The instructions provided by the measurement equipment manufacturer should be followed.

9.2.1.2 No additional guidance specified or given.

9.2.1.3 No additional guidance specified or given.

9.2.2 Installation qualification

9.2.2.1 No additional guidance specified or given.

9.2.2.2 No additional guidance specified or given.

9.2.2.3 No additional guidance specified or given.

9.2.2.4 No additional guidance specified or given.

9.2.2.5 No additional guidance specified or given.

9.2.2.6 No additional guidance specified or given.

9.3 Operational qualification

9.3.1 RH in the sterilizer chamber can be verified using a calibrated electronic sensor located at the analytical instrument sampling point of the sterilizer chamber. Analytical instruments such as gas chromatographs (GC), IR or other spectroscopic methods are less common and are more complex than the electronic sensor. Such analytical instruments can be calibrated by instrument manufacturers and the calibration should be verified after installation prior to operational qualification (OQ).

Confirmation of EO sensor calibration can be conducted in one of several ways. Some analytical instrument suppliers can provide an instruction that can be placed in the system to confirm maintenance of calibration. An alternative method is to calibrate or verify the EO sensor against known EO concentrations in a fixed volume of chamber or sample cell. There are three methods of determining EO concentration:

Method 1: use of the ideal gas law, which is based upon pressure change and temperature of EO.

Method 2: use of the fixed volume of chamber (inclusive of relevant piping and recirculation system) or sample cell and the weight of EO injected to them.

NOTE Method 1 or 2 can be used.

Method 3: comparison of measured concentration with a commercially available standard concentration of EO.

Method 1 or 2 can be used to verify calibrations if the following are confirmed:

a) correct analysis of the EO in the storage container;

b) uniform EO mixture in the chamber;

c) accurate measurement of chamber pressure;

d) accurate measurement of chamber temperature at the sampling location, weight of EO added and the volume of the chamber occupied by the EO.

Confirmation of EO concentration using either the ideal gas law and weight/volume calculations is recommended. Theoretically, in an empty chamber the three approaches (ideal gas law, weight/volume, and direct analysis) should correlate. Correlation requirements should be defined and justified by the user.

9.3.2 No additional guidance specified or given.

9.4 Performance qualification

9.4.1 General

9.4.1.1 The following should be included in the validation of sterilization processes where parametric release is used:

— the value and tolerances for chamber humidity by direct measurement during conditioning;

— the value and tolerances for the EO concentration determined from direct analysis of chamber atmosphere using analytical methods to establish the process specification during exposure time;

— temperature of the chamber; recorded from two separate monitoring locations.

NOTE See ISO 11135:2014, 9.5.5.

9.4.1.2 PQ encompasses MPQ and PPQ. The ISO 11135 requirements for MPQ are the same regardless of whether BI release or parametric release is used. ISO 11135 specifies additional requirements for PPQ when parametric release is used with respect to the determination of:

— chamber humidity by direct measurement during conditioning;

— EO concentration from direct analysis of chamber atmosphere;

— temperature of the chamber, recorded from two separate monitoring positions.

9.4.1.3 No additional guidance specified or given.

9.4.1.4 No additional guidance specified or given.

9.4.1.5 The density, composition and configuration of the load(s) used in PQ should be defined and encompass the range of density, composition and configuration of loads used in routine production. Selection of load(s) used in PQ should be justified and documented and should include consideration of maximum and minimum loading configurations.

The critical relationship between the product, packaging, load density and configuration, relative to conditions in the sterilizer, should be established during PQ and shown to be reproducible. This relationship data will be used to create the load configuration parameter for routine production cycle and parametric release. Procedures should be established to ensure that each load meets the defined load configuration parameters.

Variables such as package size, package weight, materials and pallet density should be justified and included in the validation plan.

9.4.1.6 For establishments that have widely varying load configurations, these variations should be addressed in the PQ since they can impact the measured humidity and EO concentration levels. These variations can include different load volumes, different densities or variations in the absorption characteristics of the load. Criteria for load variables such as number of pallets, weight and pallet density should be evaluated as part of the PQ to ensure that product sterility assurance level (SAL) and process parameters are not compromised.

9.4.1.7 No additional guidance specified or given.

9.4.1.8 No additional guidance specified or given.

9.4.1.9 No additional guidance specified or given.

9.4.1.10 No additional guidance specified or given.

9.4.2 Performance qualification — Microbiological

9.4.2.1 During an initial MPQ, cycles run at lower control parameters may be performed to establish the minimum routine specification requirements for EO concentration, chamber temperature and chamber humidity. When using lower control parameters, the increased probability of growth of BIs in PCDs should be considered.

Where the initial MPQ cycles were not run at lower control parameters, it might be necessary to perform additional MPQ cycle(s) to determine the minimum routine specification requirements for EO concentration, chamber temperature and chamber humidity.

9.4.2.2 No additional guidance specified or given.

9.4.2.3 No additional guidance specified or given.

9.4.2.4 No additional guidance specified or given.

9.4.2.5 No additional guidance specified or given.

9.4.2.6 No additional guidance specified or given.

9.4.3 Performance qualification — Physical

9.4.3.1 During an initial PPQ, cycles run at upper control parameters can be performed to establish the maximum routine specification requirements for EO concentration and chamber humidity.

The maximum EO concentration can be supported by the PPQ study. Where the initial PPQ cycles were not run at higher control parameters, it might be necessary to perform additional PPQ cycle(s) to determine the maximum routine specification requirements for EO concentration.

9.4.3.2 No additional guidance specified or given.

9.5 Review and approval of validation

9.5.1 The validation report should summarize the results of data gathered and the establishment of the processing specification for temperature, humidity and EO concentration (see ISO 11135:2014, 9.5.5).

NOTE Data generated from routine sterilization processes can be used to establish the variation in key process parameters and assist in the establishment of a process specification for parametric release. See Annex A.

9.5.2 No additional guidance specified or given.

9.5.3 No additional guidance specified or given.

9.5.4 No additional guidance specified or given.

9.5.5 Data should be captured to establish the following at a minimum:

a) The value and tolerances for chamber humidity by direct measurement during conditioning.

b) The value and tolerances for the EO concentration determined from direct analysis of chamber atmosphere using analytical methods to establish the process specification for routine processing. The sampling should be conducted at defined intervals sufficient to verify the required conditions throughout EO exposure.

c) The temperature of the chamber, recorded from two separate monitoring locations.

The frequency of analysis required to demonstrate that the minimum EO concentration is maintained during EO exposure should be established. Monitoring during the EO exposure time will demonstrate how the EO concentration changes over time. The results of this analysis are specific to the load configuration being analysed. The analysis performed will result in documented specifications for how often direct analysis should be performed during routine processing.

Measurement of EO concentration can be influenced by several factors, including equipment capability, process parameter uniformity and complexity of the EO mixture in the chamber. The measurement of EO and uniformity of concentrations within the chamber depend on:

a) determination of the composition and weight of the EO being added;

b) uniform mixing of the gases in the chamber (i.e. chamber circulation system, if used);

c) determination of the chamber temperature;

d) selective absorption of EO by the sterilization load.

The use of EO mixtures with diluents presents additional potential concerns. Therefore, a time delay can occur between the addition of the EO or EO mixture and the achievement of uniform EO gas concentration in the chamber, particularly if the EO is added at a single point versus a manifold or if the EO is injected into the recirculation system, if used.

Changes in measured EO concentration should be considered during the EO exposure period. This change in concentration is due to the absorption of the EO into the load with the EO concentration in the chamber equilibrating over time. This will vary depending on the load configuration, materials and the cycle design. For example, a less dense load can equilibrate quicker than a very dense load. Also, in cycles designed with an inert gas over blanket, the measured EO concentration might change after inert gas injection and then rise over the duration of the exposure.

These factors should be considered when determining the frequency of analysis. This might also include establishing an equilibration period at the start of EO exposure to allow the gas mixture in the chamber to equilibrate.

9.5.6 No additional guidance specified or given.

10 Routine monitoring and control

10.1 No additional guidance specified or given.

10.2 No additional guidance specified or given.

10.3 No additional guidance specified or given.

10.4 No additional guidance specified or given.

10.5 See ISO 11135:2014, D.10.5.

11 Product release from sterilization

11.1 For parametric release, the routine release of product as sterile is based on a demonstration of conformity of the physical processing parameters to all specifications established during the validation. Product release is based on a documented review of processing records alone rather than on documented review of processing records and BI results. Qualified individuals should perform documentation reviews.

Product release, as indicated in ISO 11135:2014, Clause 11, for parametric release cycles is equivalent to release criteria given for BI release, with the additional requirements for the review of data from a second chamber temperature sensor, humidity by direct measurement during conditioning and EO concentration by direct measurement during exposure.

If either the controlling or the monitoring sensor do not meet specification and an investigation cannot determine the accuracy of the chamber readings, the load is non-conforming.

See also ISO 11135:2014, D.11.1.

11.2 A failure investigation should be initiated to determine the cause of the non-conformity when a process variable exceeds the upper control limit or drops below the lower control limit. The product from the sterilization run should be placed on hold until an assessment of its safety can be made.

Where the control parameters are within specification but the EO, humidity data or both are out of specification, the load configuration should be included in the investigation. This can be due to the load having different absorption characteristics to the loads used during the initial validation.

Based on the outcome of the investigation, consideration can be given to continuing to process using parametric release, reverting to BI release or suspension of processing. Parametric product release can be reimplemented once appropriate correction, corrective action or both have been taken.

As many EO processes are designed to be fail-safe, it is important that release criteria consider both sterility assurance and product impact. This is critical in taking the most appropriate course of action when dealing with a process deviation. For example, if exposure time exceeds its specification due to an issue pulling the vacuum, it will result in additional lethality. Repeat processing of the load may not be the most appropriate course of action. Alternatively, the impact of the deviation might need to be evaluated for its impact on product functionality, EO residual levels or both.

If either the controlling or the monitoring sensor do not meet specification and an investigation cannot determine the accuracy of the chamber readings, the load is non-conforming.

If a failure of the temperature, humidity or EO measurement device has occurred then BI release can be used while the instrument is being repaired. Parametric release can be reimplemented after replacement or repair and recalibration of the non-conforming device.

A process that has failed to meet parametric release specification should not be released based on BI test results. Additionally, parametric release should not be used to release a process that has failed BI test results.

BI release may be used for repeat processing of the load as a substitute (or replacement) for parametric release.

11.3 No additional guidance specified or given.

11.4 No additional guidance specified or given.

12 Maintaining process effectiveness

12.1 General

12.1.1 It can be beneficial to also trend key parameters, including those for humidity and EO concentration, to confirm the process is in a state of control. This will also provide valuable data in meeting the requirement for carrying out an annual review (see ISO 11135:2014, 12.3.1) of the sterilization process.

12.1.2 The appropriate initial calibration interval and interval for routine calibration or verification should be established based on the analytical instrument manufacturer's instructions and the risk-based assessment of the performance of the analytical instrument.

The calibration of EO analytical instrument can also be performed with a replacement gas appropriate for the system if equivalence can be shown between the EO and the replacement gas over the whole concentration range of the sensor system.

12.2 Maintenance of equipment

12.2.1 No additional guidance specified or given.

12.2.2 No additional guidance specified or given.

12.2.3 No additional guidance specified or given.

12.2.4 No additional guidance specified or given.

12.3 Requalification

12.3.1 No additional guidance specified or given.

12.3.2 No additional guidance specified or given.

12.3.3 No additional guidance specified or given.

12.3.4 No additional guidance specified or given.

12.4 Assessment of change

12.4.1 If performing a PQ to change a process parameter, any statistical analysis should be repeated or a technical rationale documented to demonstrate and justify that there is no adverse impact on process as a result of the proposed change.

12.4.2 No additional guidance specified or given.

12.4.3 No additional guidance specified or given.

12.4.4 No additional guidance specified or given.

12.4.5 No additional guidance specified or given.

12.4.6 No additional guidance specified or given.

12.5 Assessment of equivalence

12.5.1 Process equivalence can be used for sterilization processes that use parametric release.

Factors that should be considered when using reduced MPQ and PPQ include:

a) the type and installation of the measuring equipment that is used to measure temperature, humidity and EO concentration;

b) the similarity in the load configuration(s) in relation to chamber volumes.

12.5.2 No additional guidance specified or given.

13 ISO 11135:2014, Annex A

No additional guidance specified or given.

14 ISO 11135:2014, Annex B

14.1 [B.1] No additional guidance specified or given.

14.2 [B.2]

14.2.1 [B.2.1] No additional guidance specified or given.

14.2.2 [B.2.2] No additional guidance specified or given.

14.2.3 [B.2.3] No additional guidance specified or given.

14.2.4 [B.2.4] When using the half cycle approach to qualify an EO process for parametric release, it is important to consider one or more of the setpoints for the temperature, humidity/steam injection and EO injection. These should be selected to establish data to support the minimum specifications for routine monitoring and control.

14.2.5 [B.2.5] When using the cycle calculation approach to qualify an EO process for parametric release, it is important to consider one or more of the setpoints for the temperature, humidity/steam injection and EO injection. These should be selected to establish data to support the minimum specifications for routine monitoring and control.