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AMENDMENT 1
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Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices

AMENDMENT 1: Revision of Annex E, Single batch release

Stérilisation des produits de santé — Oxyde d'éthylène — Exigences de développement, de validation et de contrôle de routine d'un processus de stérilisation pour des dispositifs médicaux

AMENDEMENT 1: Révision de l'Annexe E, Libération d'un lot unique

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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).

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

As a result of this amendment, the following changes have been made to Annex E:

— clarification on the application of the method i.e. for research and development of new product or for clinical trial product;

— clarification that data resulting from a single batch release study can be used to support a full validation study;

— clarification that temperature and relative humidity sensors should be used to establish conditions in the sterilization load during both the half cycle and the full cycle comprising a single batch release.

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.

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Clause 2

Correct the publication year of ISO 11138-2 from 2009 to 2006.

Add the following and also a footnote "1) Under preparation".

ISO 11138-7: —[1)] Sterilization of health care products — Biological indicators — Part 7: Guidance for the selection, use and interpretation of results

Annex E

Replace Annex E with the following:

Annex E
(normative)

Single batch release

E.1 General

This annex specifies the requirements for the release of product from a single batch for a sterilization process where there is only sufficient product, at most, for a single sterilization load, for example, during research and development of new product or for clinical trial product. This approach shall only be used to release product to market from multiple batches if it is part of a full validation. Single batch release data can be generated under either a stand-alone protocol for release of that batch, or as one part of a full validation.

NOTE The requirements of ISO 11135 apply for any aspects not specifically addressed in this annex.

E.2 Procedure

E.2.1 Assess the packaged product to determine if it can be assigned to an existing product family for sterilization purposes. This assessment considers product composition, design, packaging, bioburden and load density. The outcome of this assessment, including the rationale for decisions reached, shall be documented.

E.2.2 If the packaged product can be assigned to an existing product family refer to 12.5.2 and D.12.5.11.1.

E.2.3 Where there is no existing product family(ies), or where packaged product cannot be assigned to an existing product family, the rationale for selection and quantity of the samples shall be documented.

E.2.4 A representative number of samples taken from the manufacturing batch shall be selected for bioburden evaluation, internal PCD construction, product test of sterility, EO sterilization residuals, stability tests, functionality tests, packaging tests, biocompatibility tests, and other tests e.g. bacterial endotoxin test, as appropriate.

The number of samples selected for the product test of sterility shall be not less than that used for bioburden determination.

If comparative resistance of the internal PCD versus product bioburden has previously been assessed using a fractional cycle of shorter duration than that of the half cycle in E.2.7, there have been no positive test results from the product test of sterility samples and the bioburden testing demonstrates comparable results (numbers and types), then it is not necessary to perform the product test of sterility for product test samples exposed to the half cycle in E.2.7.

Product samples shall be randomly selected from the manufacturing batch to determine the average bioburden in accordance with ISO 11737-1.

E.2.5 Prepare internal PCDs using BIs that:

— comply with Clause 5 and 9.5 or 9.6 of ISO 11138-2:2006, plus all applicable clauses of ISO 11138-1;

— are shown to be at least as resistant to EO as is the bioburden of product to be sterilized.

If test of sterility samples are not included in the half cycle, the appropriateness of the PCD shall be documented. The PCD shall present a challenge to the sterilization process that is equivalent or greater

than the challenge presented by the natural bioburden at the most difficult to sterilize location within the product(see D.8.6 and E.2.4)

Guidance on the recommended number of internal PCDs, temperature sensors, and humidity sensors is provided in Table C.1, Table C.2, and Table C.3.

E.2.6 Distribute product test of sterility samples (if included), internal PCDs, temperature sensors, humidity sensors and other test samples (e.g. samples for EO residue tests) throughout the sterilization load, including locations where sterilizing conditions are most difficult to achieve.

E.2.7 Expose the sterilization load to a half cycle using defined process parameters selected to deliver less lethality than the specified sterilization process.

E.2.8 Remove internal PCDs and test biological indicators in accordance with manufacturer's instructions according to ISO 11138-7.

E.2.9 Remove samples for product test of sterility (if included) from the load and subject to tests of sterility in accordance with ISO 11737-2.

E.2.10 Aerate and re-equilibrate the load to ambient conditions. The aeration period shall be sufficient to allow EO residues to dissipate to a level that will not adversely affect new PCDs in the full exposure sterilization cycle (see 9.4.1.8).

E.2.11 Distribute new internal PCDs (that are the same type as used in the half cycle), temperature sensors, and humidity sensors throughout the sterilization load, including locations where sterilizing conditions are most difficult to achieve. It is recommended to use the number of internal PCDs, temperature sensors, and humidity sensors as detailed in Table C.1, Table C.2, for PQ and Table C.3 for MPQ.

E.2.12 Process the same load by exposing it to the defined sterilization process where the specified exposure time is at least double that of the half cycle in E.2.7 (i.e. a full sterilization cycle) in the same sterilization chamber.

E.2.13 Remove internal PCDs and test biological indicators in accordance with manufacturer's instructions according to ISO 11138-7.

E.2.14 Other test samples should also be removed at an appropriate time after the process (e.g. samples for residue tests, functionality tests, packaging integrity tests, biocompatibility).

E.2.15 The sterilization load can be released from sterilization if the following requirements are met:

a) confirmation that the data recorded during the half cycle meet the half cycle process specification;

b) confirmation that the data recorded during the full cycle meet the full cycle process specification;

c) confirmation of no growth of the test microorganism from internal PCDs exposed to the half cycle sterilization cycle;

d) confirmation that the appropriateness of the internal PCD versus product bioburden was successfully assessed;

This may be demonstrated by confirmation of no positive test results from product test of sterility samples (if included) exposed to a fractional cycle or the half cycle.

e) confirmation that the load has been processed by exposure to a half cycle at the specified process parameters in E.2.7 and processed again by exposure to a full sterilization cycle at specified process parameters in E.2.12;

f) confirmation of no growth of the test microorganism from internal PCDs and external PCDs (if used) exposed to the full sterilization cycle;

g) confirmation that the sterilization load humidity at the end of conditioning and sterilization load temperature during EO exposure are equivalent or greater than the minimum values achieved in the half cycle, acceptance criteria for equivalence should be documented in the protocol;

h) confirmation that product functionality, stability, biocompatibility, and package integrity comply with the specified requirements after exposure to both the full sterilization cycle and the half cycle (see 7.2.1 – the rationale for the extent of product definition testing shall be documented);

i) confirmation that product EO sterilization residual levels comply with the requirements of ISO 10993-7 after sequential exposure to both the full sterilization cycle and the half cycle.

NOTE There is no requirement to evaluate EO sterilization residual levels after the half cycle only.

Information and data generated from this approach can be used at a later time to support future definition of the sterilization process as indicated in this standard.

