DRAFT INTERNATIONAL STANDARD

ISO/DIS 14160

ISO/TC **198**	Secretariat: **ANSI**
Voting begins on: **2018-04-26**	Voting terminates on: **2018-07-19**

Sterilization of health care products — Liquid chemical sterilizing agents for single-use medical devices utilizing animal tissues and their derivatives — Requirements for characterization, development, validation and routine control of a sterilization process for medical devices

Stérilisation des produits de santé — Agents stérilisants chimiques liquides pour dispositifs médicaux non réutilisables utilisant des tissus animaux et leurs dérivés — Exigences pour la caractérisation, le développement, la validation et le contrôle de routine d'un procédé de stérilisation de dispositifs médicaux

ICS: 11.080.01

This document is circulated as received from the committee secretariat.

ISO/CEN PARALLEL PROCESSING

Reference number
ISO/DIS 14160:2018(E)

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Published in Switzerland

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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.

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 on 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 the following URL: www.iso.org/iso/foreword.html.

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

This third edition cancels and replaces the second edition (ISO 14160:2011), which has been technically revised.

The main changes compared to the previous edition are as follows:

— aligned definitions with those used in other standards for development, validation and routine control of sterilization processes and added new definitions;

— incorporated defined terms consistently throughout the document;

— updated cross-references;

— revised Informative Annex A to follow the order of the normative body of the standard;

— added clarification to Normative Annex B in regards to applying the overkill approach.

A list of all parts in the ISO 14160 series can be found on the ISO website.

Introduction

A sterile medical device is one that is free of viable microorganisms. International standards, which specify requirements for validation and routine control of sterilization processes, require, when it is necessary to supply a sterile medical device, that adventitious microbiological contamination of a medical device prior to sterilization be minimized. Even so, medical devices produced under standard manufacturing conditions in accordance with the requirements for quality management systems (see, for example, ISO 13485) can, prior to sterilization, have microorganisms on them, albeit in low numbers. The purpose of sterilization is to inactivate the microbiological contaminants and thereby transform the non-sterile medical devices into sterile ones.

The kinetics of inactivation of a pure culture of microorganisms by physical and/or chemical agents used to sterilize medical devices can generally best be described by an exponential relationship between the numbers of microorganisms surviving and the extent of treatment with the sterilizing agent; inevitably this means that there is always a finite probability that a microorganism survives regardless of the extent of treatment applied. For a given treatment, the probability of survival is determined by the number and resistance of microorganisms and by the environment in which the organisms exist during treatment. It follows that the sterility of any one medical device in a population of items subjected to sterilization processing cannot be guaranteed and the sterility of a processed population is defined in terms of the probability of there being a viable microorganism present on a medical device.

Attention also has to be given to a number of factors, including the microbiological status (bioburden) of incoming raw materials and/or components and their subsequent storage, and to the control of the environment in which the product is manufactured, assembled and packaged (see also ISO 13485).

Requirements for quality management systems for medical device production are given in ISO 13485. The standards for quality management systems recognize that, for certain processes used in manufacturing, the effectiveness of the process cannot be fully verified by subsequent inspection and testing of the product. Sterilization is an example of such a process. For this reason, sterilization processes are validated for use, the performance of the sterilization process is monitored routinely and the equipment is maintained.

Animal tissues and their derivatives are used as constituents of certain medical devices to provide performance characteristics that present advantages over the characteristics provided by non-animal-based materials. The range and quantities of materials of animal origin in medical devices vary; such materials can comprise a major part of the device, can be a product coating or impregnation, or can be used in the manufacturing process for the medical device.

This International Standard describes requirements that, if met, will provide a liquid chemical sterilization process that has appropriate microbicidal activity for single-use medical devices containing materials of animal origin or their derivatives. The sterilizing agents used most frequently for medical devices are moist heat, dry heat, irradiation and ethylene oxide. While some devices containing animal tissues can be compatible with these commonly applied methods of sterilization (historically, for example, catgut sutures have been sterilized by irradiation), other devices, such as biological heart valves or tissue patches, are not compatible with conventional sterilization processes. It has been recognized that other sterilizing agents might have to be used in these exceptional circumstances. Liquid chemical sterilization is normally chosen over other sterilization processes in order that the medical devices present the desired physical properties of the tissue after sterilization. Sterilization by liquid chemicals of medical devices made in whole or in part from tissues of animal origin represents a special case in terms of establishing an effective sterilization process. In common with the other sterilization methods, the efficacy of a liquid chemical sterilization process needs to be demonstrated and recorded before it is adopted for routine use.

Liquid chemical sterilization requires determination of types of microorganisms comprising the bioburden and their resistance to the sterilization process in order to establish the appropriate reference microorganism, whether that be a recognized biological indicator or an isolate from the bioburden. Compliance with the requirements of this International Standard ensures that the microbicidal activity of the liquid chemical sterilization process is both reliable and reproducible so that predictions can be made, with reasonable confidence, that there is a low level of probability of there being a viable

microorganism present on a product after sterilization. Specification of this probability is a matter for regulatory authorities and can vary among regions or countries (see, for example, EN 556-1 and ANSI/AAMI ST67).

Exposure to a properly validated, accurately controlled sterilization process is not the only factor associated with the provision of reliable assurance that the product is sterile and, in this regard, suitable for its intended use. Attention is therefore given to a number of considerations including:

a) the source and harvesting conditions of the tissue;

b) the microbiological status of incoming raw materials or components, or both;

c) the routine control of any cleaning and disinfection procedures used on the product;

d) the control of the environment in which the product is manufactured, assembled and packaged;

e) the control of equipment and processes;

f) the control of personnel and their hygiene;

g) the manner and materials in which the product is packaged; and

h) the conditions under which product is stored.

Sterilization of health care products — Liquid chemical sterilizing agents for single-use medical devices utilizing animal tissues and their derivatives — Requirements for characterization, development, validation and routine control of a sterilization process for medical devices

1 Scope

This document specifies requirements for the characterization of a liquid chemical sterilizing agent and for the development, validation, process control and monitoring of sterilization by liquid chemical sterilizing agents of single-use medical devices comprising, in whole or in part, materials of animal origin.

This document covers the control of risks arising from contamination with bacteria and fungi by application of a liquid chemical sterilization process. Risks associated with other microorganisms can be assessed using other methods (see Note 1).

This document is not applicable to material of human origin.

This document does not describe methods for the validation of the inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents (see Note 2 and Note 3).

This document does not describe methods for validation of the inactivation or elimination of protozoa and parasites.

The requirements for validation and routine control described in this document are only applicable to the defined sterilization process of a medical device, which is performed after the manufacturing process, and do not take account of the lethal effects of other bioburden reduction steps (see Note 4).

This document does not specify tests to establish the effects of any chosen sterilization process upon the fitness for use of the medical device (see Note 5).

This document does not cover the level of residual sterilizing agent within medical devices (see Note 6).

This document does not describe a quality management system for the control of all stages of manufacture (see Note 7).

NOTE 1 The prior application of risk management principles to medical devices utilizing animal tissues, as described in ISO 22442-1, is important.

NOTE 2 Liquid chemical sterilizing agents traditionally employed to sterilize animal tissues in medical devices might not be effective in inactivating the causative agents of TSE such as bovine spongiform encephalopathy (BSE), or scrapie. Satisfactory validation in accordance with this document does not necessarily demonstrate inactivation of infective agents of this type. Risk controls related to sourcing, collection and handling of animal materials are described in ISO 22442-2.

NOTE 3 The validation of the inactivation, elimination, or elimination and inactivation of viruses and TSE agents is described in ISO 22442-3.

NOTE 4 Manufacturing processes for medical devices containing animal tissues frequently include exposure to chemical agents which can significantly reduce the bioburden on the medical device. Following the manufacturing process, a medical device is exposed to a defined sterilization process.

NOTE 5 Such testing is a crucial part of the design and development of a medical device.

NOTE 6 ISO 10993-17 specifies a method to establish allowable limits for residues of sterilizing agents.

NOTE 7 Standards for quality management systems (see ISO 13485) can be used in the control of all stages of manufacture including the sterilization 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 10012, *Measurement management systems — Requirements for measurement processes and measuring equipment*

ISO 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 10993-17, *Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances*

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

ISO 13408-7, *Aseptic processing of health care products — Part 7: Alternative processes for medical devices and combination products devices and combination products*

ISO 13485:2016, *Medical devices — Quality management systems — Requirements for regulatory purposes*

ISO 22442-2, *Medical devices utilizing animal tissues and their derivatives — Part 2: Controls on sourcing, collection and handling*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

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

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

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

3.1
batch
defined quantity of product, intended or purported to be uniform in character and quality, which has been produced during a defined cycle of manufacture

[SOURCE: ISO/DIS 11139:2017, 3.21]

3.2
bioburden
population of viable microorganisms on or in product and/or sterile barrier system

[SOURCE: ISO/DIS 11139:2017, 3.23]

3.3
carrier
<biological indicator> supporting material on or in which test microorganisms are deposited

[SOURCE: ISO/DIS 11139:2017, 3.33]

3.4
D value
D_{10} value
time or radiation dose required under stated conditions to achieve inactivation of 90 % of a population of the test microorganisms

[SOURCE: ISO/DIS 11139:2017, 3.77]

3.5
holding time
period during which process parameters are maintained in the load, within their specified tolerances

[SOURCE: ISO/DIS 11139:2017, 3.133]

3.6
inactivation
see microbial inactivation (3.12)

3.7
inactivation curve
graphical representation of inactivation of a population of microorganisms with increasing exposure to a microbicidal agent under stated conditions

[SOURCE: ISO/DIS 11139:2017, 3.137]

3.8
inoculated carrier
supporting material on or in which a defined number of viable test organisms have been deposited

[SOURCE: ISO/DIS 11139:2017, 3.144]

3.9
installation qualification
IQ
process of establishing by objective evidence that all key aspects of the process equipment and ancillary system installation adhere to the approved specification

[SOURCE: ISO DIS 11139:2017, 3.223.2]

3.10
liquid chemical sterilizing agent
liquid chemical entity, or combination of entities, having sufficient microbicidal activity to achieve sterility under defined conditions

3.11
medical device
instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use or calibrator, software, material or other similar related article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific medical purpose(s) of:

— diagnosis, prevention, monitoring, treatment or alleviation of disease;

— diagnosis, monitoring, treatment, alleviation of or compensation for an injury;

— investigation, replacement, modification or support of the anatomy or of a physiological process;

— supporting or sustaining life;

— control of conception;

— disinfection of medical devices;

— providing information by means of in vitro examination of specimens derived from the human body;

and does not achieve its primary intended action by pharmacological, immunological or metabolic means, butwhich may be assisted in its intended function by such means

Note 1 to entry: Products which may be considered to be medical devices in some jurisdictions but not in others include:

— items specifically intended for cleaning, packaging, or sterilization of medical devices

— disinfection substances;

— aids for persons with disabilities;

— devices incorporating animal and/or human tissues;

— devices for in vitro fertilization or assisted reproduction technologies.

[SOURCE: ISO/DIS 11139:2017, 3.166]

3.12
microbial inactivation
loss of ability of microorganisms to grow and/or multiply

3.13
operational qualification
OQ
process of obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with its operational procedures

[SOURCE: ISO/DIS 11139:2017, 3.223.3]

3.14
parametric release
declaration that product is sterile, based on records demonstrating that the process parameters were delivered within specified tolerances

[SOURCE: ISO/DIS 11139:2017, 3.193]

3.15
performance qualification
PQ
process of establishing by objective evidence that the process, under anticipated conditions, consistently produces a product which meets all predetermined requirements

[SOURCE: ISO/DIS 11139:2017, 3.223.4]

3.16
product family
group or subgroup of product characterized by similar attributes determined to be equivalent for evaluation and processing purposes

[SOURCE: ISO/DIS 11139:2017, 3.220]

3.17
requalification
repetition of part of validation for the purpose of confirming the continued acceptability of a specified process

[SOURCE: ISO/DIS 11139:2017, 3.235]