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**Sterilization of health care products —  
General requirements for characterization  
of a sterilizing agent and the  
development, validation and routine  
control of a sterilization process for  
medical devices**

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*Stérilisation des produits de santé — Exigences générales pour la  
caractérisation d'un agent stérilisant et pour la mise au point, la  
validation et la vérification de routine d'un processus de stérilisation  
pour dispositifs médicaux*

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Case postale 56 • CH-1211 Geneva 20  
Tel. + 41 22 749 01 11  
Fax + 41 22 749 09 47  
E-mail [copyright@iso.org](mailto:copyright@iso.org)  
Web [www.iso.org](http://www.iso.org)

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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.

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 14937 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

This second edition cancels and replaces the first edition (ISO 14937:2000) and ISO 14937:2000/Cor.1:2003 which have been technically revised.

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## Introduction

A sterile medical device is one that is free of viable microorganisms. International Standards that 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) could, prior to sterilization, have microorganisms on them, albeit in low numbers. Such medical devices are non-sterile. 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 generally can best be described by an exponential relationship between the number 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 might survive 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 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.

This International Standard describes requirements that, if met, will provide a sterilization process with appropriate microbicidal activity intended to sterilize medical devices. Furthermore, compliance with the requirements ensures that the 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 medical device after sterilization. Specification of this probability is a matter for regulatory authorities and can vary from country to country (see, for example, EN 556-1 and ANSI/AAMI ST67).

Generic requirements of the quality management system for design and development, production, installation and servicing are given in ISO 9001 and particular requirements for quality management systems for medical device production are given in ISO 13485. The standards for quality management systems recognise 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.

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

- a) the microbiological status of incoming raw materials and/or components;
- b) the validation and routine control of any cleaning and disinfection procedures used on the medical device;
- c) the control of the environment in which the medical device is manufactured, assembled and packaged;
- d) the control of equipment and processes;
- e) the control of personnel and their hygiene;
- f) the manner and materials in which the medical device is packaged;
- g) the conditions under which the medical device is stored.

The type of contamination on a medical device to be sterilized varies, and this influences the effectiveness of a sterilization process. Medical devices that have been used in a health care setting and that are being presented for resterilization in accordance with the manufacturer's instructions (see ISO 17664) should be regarded as special cases. There is the potential for such medical devices to possess a wide range of contaminating microorganisms and residual inorganic and/or organic contamination in spite of the application of a cleaning process. Hence, particular attention has to be given to the validation and control of the cleaning and disinfection processes used during reprocessing.

The requirements are the normative parts of this International Standard with which compliance is claimed. The guidance given in Annex E is not normative and is not provided as a checklist for auditors. The guidance provides explanations and methods that are regarded as being a suitable means for complying with the requirements. Methods other than those given in the guidance can be used if they are effective in achieving compliance with the requirements of this International Standard.

The development, validation and routine control of a sterilization process comprise a number of discrete but interrelated activities, for example, calibration, maintenance, product definition, process definition, installation qualification, operational qualification and performance qualification. While the activities required by this International Standard have been grouped together and are presented in a particular order, this International Standard does not require that the activities be performed in the order that they are presented. The activities required are not necessarily sequential, as the programme of development and validation can be iterative. The responsibility for carrying out the activities required by this International Standard will vary from case to case. This International Standard requires that the responsibilities of the various parties be defined (see 4.2) but does not specify to whom the responsibilities are allocated. Annex E provides guidance on allocation of responsibility.

This International Standard has three distinct applications:

- for manufacturers of health care products who wish to apply to their products a sterilization process for which a specific International Standard does not exist;
- for manufacturers and users of sterilization processes in health care settings for which a specific International Standard does not exist;
- as a framework for the preparation or revision of standards for specific sterilization processes.

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# Sterilization of health care products — General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices

## 1 Scope

### 1.1 Inclusions

**1.1.1** This International Standard specifies general requirements for the characterization of a sterilizing agent and for the development, validation and routine monitoring and control of a sterilization process for medical devices.

**NOTE** Although the scope of this International Standard is limited to medical devices, the requirements specified herein can also be applied to sterilization processes for other health care products.

**1.1.2** This International Standard applies to sterilization processes in which microorganisms are inactivated by physical and/or chemical means.

**1.1.3** This International Standard is intended to be applied by process developers, manufacturers of sterilization equipment, manufacturers of medical devices to be sterilized, and organizations responsible for sterilizing medical devices.

**1.1.4** This International Standard specifies the elements of a Quality Management System which are necessary to assure the appropriate characterization of the sterilizing agent, development, validation and routine monitoring and control of a sterilization process.

**NOTE** It is not a requirement of this International Standard to have a full quality management system. The necessary elements are normatively referenced at appropriate places in the text (see, in particular, Clause 4). Attention is drawn to the standards for quality management systems (see ISO 13485) that control all stages of production or reprocessing of medical devices. National and/or regional regulations for the provision of medical devices might require the implementation of a full quality management system and the assessment of that system by a third party.

### 1.2 Exclusions

**1.2.1** This International Standard does not apply to sterilization processes that rely solely on physical removal of microorganisms (for example, filtration).

**1.2.2** This International Standard does not describe detailed procedures for assessing microbial inactivation.

**1.2.3** This International Standard does not specify requirements for characterization of an agent or for development, validation and routine control of a process for inactivating the causative agents of spongiform encephalopathies such as scrapie, bovine spongiform encephalopathy and Creutzfeldt-Jakob disease. Specific recommendations have been produced in particular countries for the processing of materials potentially contaminated with these agents.

**NOTE** See also ISO 22442-1, ISO 22442-2 and ISO 22442-3.

**1.2.4** This International Standard does not supersede or modify published International Standards for particular sterilization processes.

## 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 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 11138-1:2006, *Sterilization of health care products — Biological indicators — Part 1: General requirements*

ISO 11140-1, *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 11737-2, *Sterilization of medical devices — Microbiological methods — Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process*

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

IEC 61010-2-040, *Safety requirements for electrical equipment for measurement, control and laboratory use — Part 2-040: Particular requirements for sterilizers and washer-disinfectors used to treat medical materials*

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## 3 Terms and definitions

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

### 3.1

#### **bioburden**

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

[ISO/TS 11139:2006, definition 2.2]

### 3.2

#### **biological indicator**

test system containing viable microorganisms providing a defined resistance to a specified sterilization process

[ISO/TS 11139:2006, definition 2.3]

### 3.3

#### **change control**

assessment and determination of the appropriateness of a proposed alteration to product or procedure

[ISO/TS 11139:2006, definition 2.5]

**3.4****chemical indicator****non-biological indicator**

test system that reveals change in one or more pre-defined process variables based on a chemical or physical change resulting from exposure to a process

[ISO/TS 11139:2006, definition 2.6]

**3.5****corrective action**

action to eliminate the cause of a detected non-conformity or other undesirable situation

NOTE 1 There can be more than one cause for a non-conformity.

NOTE 2 Corrective action is taken to prevent recurrence whereas **preventive action** (3.17) is taken to prevent occurrence.

NOTE 3 There is a distinction between **correction** (3.6) and corrective action.

[ISO 9000:2005, definition 3.6.5]

**3.6****correction**

action to eliminate a detected non-conformity

NOTE A correction can be made in conjunction with a **corrective action** (3.5).

[ISO 9000:2005, definition 3.6.6]

**3.7****development**

act of elaborating a specification

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[ISO/TS 11139:2006, definition 2.13]

**3.8****establish**

determine by theoretical evaluation and confirm by experimentation

[ISO/TS 11139:2006, definition 2.17]

**3.9****fault**

one or more of the process parameters lying outside of its/their specified tolerance(s)

[ISO/TS 11139:2006, definition 2.19]

**3.10****health care product(s)**

medical device(s), including *in vitro* diagnostic medical device(s), or medicinal product(s), including biopharmaceutical(s)

[ISO/TS 11139:2006, definition 2.20]

**3.11**  
**installation qualification**  
**IQ**

process of obtaining and documenting evidence that equipment has been provided and installed in accordance with its specification

[ISO/TS 11139:2006, definition 2.22]

**3.12**  
**material safety data sheet**  
**MSDS**

document specifying the properties of a substance, its potential hazardous effects for humans and the environment, and the precautions necessary to handle and dispose of the substance safely

[ISO/TS 11139:2006, definition 2.23]

**3.13**  
**medical device**

instrument, apparatus, implement, machine, appliance, implant, *in vitro* reagent or calibrator, software, material or other related article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific 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, <https://standards.iteh.ai/catalog/standards/sist/06334363-8af2-48eb-b0f2-ba233d9b70c9/iso-14937-2009>
- disinfection of medical devices,
- providing information for medical purposes by means of *in vitro* examination of specimens derived from the human body

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and which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means

[ISO 13485:2003, definition 3.7]

NOTE This definition from ISO 13485:2003 has been developed by the Global Harmonization Task Force (GHTF 2002).

**3.14**  
**operational qualification**  
**OQ**

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

[ISO/TS 11139:2006, definition 2.27]

**3.15**  
**parametric release**

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

[ISO/TS 11139:2006, definition 2.29]

**3.16****performance qualification****PQ**

process of obtaining and documenting evidence that the equipment, as installed and operated in accordance with operational procedures, consistently performs in accordance with predetermined criteria and thereby yields product meeting specifications

[ISO/TS 11139:2006, definition 2.30]

**3.17****preventive action**

action to eliminate the cause of a potential non-conformity or other undesirable potential situation

NOTE 1 There can be more than one cause for a potential non-conformity.

NOTE 2 Preventive action is taken to prevent occurrence, whereas **corrective action** (3.5) is taken to prevent recurrence.

[ISO 9000:2005, definition 3.6.4]

**3.18****process challenge device****PCD**

item designed to constitute a defined resistance to a sterilization process and used to assess performance of the process

[ISO/TS 11139:2006, definition 2.33]

**3.19****process parameter**

specified value for a process variable

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NOTE The specification for a sterilization process includes the process parameters and their tolerances.

[ISO/TS 11139:2006, definition 2.34]

**3.20****process variable**

condition within a sterilization process, changes in which alter microbicidal effectiveness

EXAMPLES Time, temperature, pressure, concentration, humidity, wavelength.

[ISO/TS 11139:2006, definition 2.35]

**3.21****recognised culture collection**

depository authority under the Budapest Treaty on *The International Recognition of the Deposit of Microorganisms for the Purpose of Patent and Regulation*

[ISO/TS 11139:2006, definition 2.38]

**3.22****reference microorganism**

microbial strain obtained from a recognised culture collection

[ISO/TS 11139:2006, definition 2.39]